삼광의료재단
서울특별시 서초구 바우뫼로41길 58 (양재동, 선화빌딩)
검사기관 11365200
Tel. 1661-5117
www.smlab.co.kr

Patient Name: 이현희
Gender: Female
Sample ID: N26-90

Primary Tumor Site: endometrium
Collection Date: 2026.02.25

Sample Cancer Type: Endometrial Carcinoma

Report Highlights

3 Relevant Biomarkers
1 Therapies Available
10 Clinical Trials

Relevant Endometrial Carcinoma Findings

Gene	Finding
BRAF	None detected
ERBB2	None detected
NTRK1	None detected
NTRK2	None detected
NTRK3	None detected
RET	None detected

Genomic Alteration	Finding
Microsatellite Status	***Microsatellite stable***
Tumor Mutational Burden	***2.85 Mut/Mb measured***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*AKT1 p.(E17K) c.49G>A* AKT serine/threonine kinase 1 Allele Frequency: 72.09% Locus: chr14:105246551 Transcript: NM_001014431.2	None*	**capivasertib + hormone therapy** [1, 2 / II +]	7
IIC	*ARID1A deletion* AT-rich interaction domain 1A Locus: chr1:27022875	None*	None*	2
IIC	*CTNNB1 p.(T41I) c.122C>T* catenin beta 1 Allele Frequency: 32.42% Locus: chr3:41266125 Transcript: NM_001904.4	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.

Prevalent cancer biomarkers without relevant evidence based on included data sources

*ESR1::TFG fusion, MTOR p.(M2327I) c.6981G>A, Microsatellite stable, USP9X p.(D134Afs*8) c.401_406delATGAAGinsC, SPEN deletion, EPHA2 deletion, HLA-B deletion, MTAP::CDKN2B-AS1-004 fusion, CTCF deletion, CDH1 deletion, ZFHX3 deletion, CYP2D6 c.506-1G>A, Tumor Mutational Burden*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
AKT1	p.(E17K)	c.49G>A	COSM33765	chr14:105246551	72.09%	NM_001014431.2	missense
CTNNB1	p.(T41I)	c.122C>T	COSM5676	chr3:41266125	32.42%	NM_001904.4	missense
MTOR	p.(M2327I)	c.6981G>A	COSM1662881	chr1:11177096	35.35%	NM_004958.4	missense
USP9X	p.(D134Afs*8)	c.401_406delATGAAGinsC	.	chrX:40994056	34.90%	NM_001039590.3	frameshift Block Substitution
CYP2D6	p.(?)	c.506-1G>A	COSM5019461	chr22:42524947	44.56%	NM_000106.6	unknown
USP9X	p.(T133P)	c.397A>C	.	chrX:40994052	34.76%	NM_001039590.3	missense
USP9X	p.(V137_W140delinsL)	c.409_420delGTGAGTGGCTGGinsCTC	.	chrX:40994064	35.51%	NM_001039590.3	nonframeshift Block Substitution

Gene Fusions

Genes	Variant ID	Locus
ESR1::TFG	ESR1-TFG.E6T4	chr6:152265643 - chr3:100447556
MTAP::CDKN2B-AS1-004	MTAP-CDKN2B	chr9:21838009 - chr9:22046750

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
ARID1A	chr1:27022875	1.03	0.65
SPEN	chr1:16174516	0.99	0.64
EPHA2	chr1:16451707	1.14	0.69
HLA-B	chr6:31322252	0.73	0.55
CTCF	chr16:67644720	0.96	0.63
CDH1	chr16:68771249	1.03	0.65
ZFHX3	chr16:72820995	0.87	0.6

Biomarker Descriptions

AKT1 p.(E17K) c.49G>A

AKT serine/threonine kinase 1

Background: The AKT1 gene encodes Protein Kinase B, a serine/threonine kinase, that belongs to a family of closely related protein kinases that also includes AKT2 and AKT3. Growth factor signaling leads to the activation of phosphatidylinositol 3-kinase (PI3K),

Biomarker Descriptions (continued)

recruitment of AKT to the plasma membrane, and subsequent activation of downstream effectors including MTOR. The PI3K/AKT/MTOR pathway is central to the regulation of cancer cell proliferation, survival, and metabolism[61,62].

Alterations and prevalence: AKT1 encodes a proto-oncogene that is the target of recurrent somatic mutations in cancer[63]. The most common recurrent mutation is E17K, which is located in the N-terminal pleckstrin homology (PH) domain. E17K is a gain-of-function activating mutation that constitutively targets AKT1 to the plasma membrane and leads to downstream signaling[64,65]. Other recurrent activating mutations include L52H, Q79K, and D323Y/G/N, which disrupt negative regulatory interactions between the PH domain and the kinase domain[66]. AKT1 mutations in cancer are common in breast and endometrial cancers, where they occur at a prevalence of 2-5%[15]. AKT1 mutations are observed at a prevalence of 1-2% in bladder, colorectal, melanoma, and thyroid cancers[15,16]. AKT1 is overexpressed via gene amplification in ovarian cancer, lung squamous cell cancer, and sarcoma at a prevalence of 2-5%[15,16].

Potential relevance: Currently no therapies are approved for AKT1 aberrations. However, in the phase II NCI-MATCH trial, the pan-AKT inhibitor capivasertib (AZD5363) demonstrated a partial response in 23% (8/35) of AKT1 E17K mutated solid tumor patients[67]. Results from a phase I clinical trial of capivasertib demonstrated partial responses in 9/52 heavily pre-treated patients with AKT1 E17K mutated solid tumors, with a median progression-free survival (PFS) of 5.5 months in ER positive breast cancer, 6.6 months in gynecologic cancers, and 4.2 months in other solid tumors[68]. In the same phase I study, an ovarian cancer patient with an AKT1 Q79K mutation demonstrated stable disease lasting 14 months[68].

ARID1A deletion

AT-rich interaction domain 1A

Background: The ARID1A gene encodes the AT-rich interaction domain 1A tumor suppressor protein[21]. ARID1A, also known as BAF250A, belongs to the ARID1 subfamily that also includes AR1D1B[21,34]. ARID1A and ARID1B are mutually exclusive subunits of the BAF variant of the SWI/SNF chromatin-remodeling complex[34,35]. The BAF complex is a multisubunit protein that consists of SMARCB1/IN1, SMARCC1/BAF155, SMARCC2/BAF170, SMARCA4/BRG1 or SMARCA2/BRM, and ARID1A or ARID1B[35]. The BAF complex remodels chromatin at promoter and enhancer elements to alter and regulate gene expression[35,36]. ARID1A binds to transcription factors and coactivator/corepressor complexes to alter transcription[34]. Recurrent inactivating mutations in BAF complex subunits, including ARID1A, lead to transcriptional dysfunction thereby, altering its tumor suppressor function[34].

Alterations and prevalence: Mutations in SWI/SNF complex subunits are the most commonly mutated chromatin modulators in cancer and have been observed in 20% of all tumors[36]. The majority of ARID1A inactivating mutations are nonsense or frameshift mutations[34]. Somatic mutations in ARID1A have been identified in several cancers including 50% of ovarian clear cell carcinoma, 30% of endometrioid carcinoma, and 24-43% of uterine corpus endometrial carcinoma, bladder urothelial carcinoma, and stomach adenocarcinoma[15,16,35]. In microsatellite stable (MSS) colorectal cancer, mutations in ARID1A have been observed to correlate with increased tumor mutational burden (TMB) and expression of genes involved in the immune response[37]. Biallelic deletion of ARID1A is observed in 3% of cholangiocarcinoma and stomach adenocarcinoma, and 2% of pheochromocytoma and paraganglioma[15,16]. Alterations in ARID1A are also observed in pediatric cancers[16]. Somatic mutations in ARID1A are observed in 12% of non-Hodgkin lymphoma (2 in 17 cases), 8% of Hodgkin lymphoma (5 in 61 cases), 5% of T-lymphoblastic leukemia/lymphoma (2 in 41 cases), 3% of soft tissue sarcoma (1 in 38 cases), 2% of embryonal tumors (5 in 332 cases), 1% of glioma (4 in 297 cases), and less than 1% of bone cancer (3 in 327 cases), B-lymphoblastic leukemia/lymphoma (1 in 252 cases), and peripheral nervous system tumors (2 in 1158 cases)[16]. Biallelic deletion of ARID1A is observed in 2% of peripheral nervous system cancers (2 in 91 cases), 1% of leukemia (3 in 250 cases), and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases)[16].

Potential relevance: Currently, no therapies are approved for ARID1A aberrations. However, the FDA has granted fast track designation (2022) to HSF1 pathway inhibitor, NXP-800[38], for the treatment of platinum resistant ARID1A-mutated ovarian carcinoma. Tulmimetostat[39], dual inhibitor of EZH2 and EZH1, was also granted a fast track designation (2023) for the treatment of patients with advanced, recurrent or metastatic endometrial cancer harboring ARID1A mutations and who have progressed on at least one prior line of treatment.

CTNNB1 p.(T41I) c.122C>T

catenin beta 1

Background: The CTNNB1 gene encodes catenin beta-1 (β-catenin), an integral component of cadherin-based adherens junctions, which are involved in maintaining adhesion and regulating the growth of epithelial cell layers[1]. CTNNB1 binds to the APC protein in the cytoplasm and interacts with TCF and LEF transcription factors in the nucleus to regulate WNT signaling[2]. Steady-state levels of CTNNB1 are regulated by ubiquitin-dependent proteolysis[3,4,5]. CTNNB1 exon 3 mutations can lead to persistent activation of the WNT/β-catenin pathway and alter downstream nuclear transcription[6].

Alterations and prevalence: Recurrent somatic mutations leading to CTNNB1 activation are common in cancer. The most prevalent alterations include missense mutations in exon 3 at codons S33, S37, T41, and S45 that block phosphorylation by GSK-3β and inhibit CTNNB1 degradation[6,7,8,9]. These activating mutations are observed in diverse solid tumors and have a prevalence of 20-30% in

Biomarker Descriptions (continued)

hepatocellular carcinoma, 20% in uterine carcinoma, and 15% in adrenocortical carcinoma[10,11,12,13,14,15,16]. Alterations in CTNNB1 are also observed in pediatric cancers[15,16]. Somatic mutations are observed in 36% of hepatobiliary cancer (4 in 11 cases), 6% of embryonal tumor (21 in 332 cases), 3% of soft tissue sarcoma (1 in 38 cases), 2% of Wilms tumor (11 in 710 cases), and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases) and bone cancer (1 in 327 cases)[15,16].

Potential relevance: Currently, no therapies have been approved for CTNNB1 aberrations. CTNNB1 alterations have been proposed to promote cancer progression and limit the response to EGFR tyrosine kinase inhibitors in EGFR mutant lung cancer[17]. Mutation of CTNNB1 is considered an ancillary diagnostic biomarker for desmoid fibromatosis and WNT-activated medulloblastoma[18,19,20].

ESR1::TFG fusion

TRK-fused gene, estrogen receptor 1

Background: The ESR1 gene encodes estrogen receptor 1 (ERα), which is a member of the superfamily of nuclear receptors which convert extracellular signals into transcriptional responses[21]. A related gene, ESR2, encodes the cognate ERβ protein[21]. ERα is a ligand-activated transcription factor regulated by the hormone estrogen[69,70]. Estrogen binding to ERα results in receptor dimerization, nuclear translocation, and target gene transcription. In addition, estrogen binding to the ERα results in the activation of the RAS/RAF/MEK/ERK, PI3K/AKT/mTOR, cAMP/PKA and PLC/PKC signaling pathways and cell proliferation and survival[71]. In neuroblastoma, MYCN-driven miR-17~92 cluster expression suppresses ESR1 to block differentiation, whereas estrogen-activated ESR1 cooperates with ETS-1 to promote MMP1/9 expression and tumor proliferation, migration, and invasion[72,73].

Alterations and prevalence: Approximately 70% of breast cancers express ERα and ERβ positivity. Mutations in the ERα ligand binding domain, including S463P, Y537S, and D538G, result in endocrine-independent constitutive receptor activation, which is a common mechanism of endocrine resistance[74,75,76,77]. Somatic mutations in ESR1 are observed in 5% of uterine corpus endometrial carcinoma, 4% of colorectal adenocarcinoma and skin cutaneous melanoma, 3% of stomach adenocarcinoma, and 2% of lung adenocarcinoma, lung squamous cell carcinoma, and esophageal adenocarcinoma[15,16]. ESR1 gene fusions and ESR1 copy number gains have also been observed and are associated with advanced endocrine resistant disease[78,79,80,81,82]. Amplification of ESR1 is observed in 5% of uterine carcinosarcoma, 4% of sarcoma, 3% of uterine corpus endometrial carcinoma, and 2% of ovarian serous cystadenocarcinoma, adrenocortical carcinoma, and breast invasive carcinoma[15,16]. Alterations in ESR1 are also observed in pediatric cancers[83]. Somatic mutations in ESR1 are observed in 5% of T-lymphoblastic leukemia/lymphoma (2 in 41 cases), 1% of glioma (3 in 297 cases), and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases), leukemia (1 in 311 cases), and peripheral nervous system cancers (1 in 1158 cases)[83]. Amplification of ESR1 is observed in less than 1% of leukemia (1 in 250 cases)[83].

Potential relevance: The FDA has approved elacestrant[84] (2023) for the treatment of postmenopausal women or adult men with ER-positive/ERBB2-negative, ESR1-mutated advanced or metastatic breast cancer[85]. The FDA also approved imlunestrant[86] (2025) for the treatment of adults with ER-positive, HER2-negative, ESR1-mutated advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy. The FDA has also granted fast track designations to the following therapies: AC-699[87] (2024) and lasofoxifene[88] (2019) for ESR1-mutated, ER-positive/ERBB2-negative metastatic breast cancer, camizestrant[89] for ESR1-mutated, HR-positive/ERBB2-negative metastatic breast cancer, and seviteronel[90] (2016) for ER-positive breast cancer. Anti-estrogen (endocrine) treatments such as tamoxifen[91] (1977), fulvestrant[92] (2002), letrozole[93] (1995), and exemestane[94] (2005) are FDA approved for ER-positive metastatic breast cancers[95,96]. Although ERα and ERβ positivity predicts response to endocrine therapies, about a quarter of patients with primary breast cancer and almost all patients with metastatic disease will develop endocrine resistance[97,98,99].

MTOR p.(M2327I) c.6981G>A

mechanistic target of rapamycin

Background: The MTOR gene encodes the mechanistic target of rapamycin kinase (also known as, mammalian target of rapamycin), which is a member of the phosphatidylinositol 3-kinase (PI3K)-related kinases family of serine/threonine protein kinases[21]. MTOR encodes the catalytic subunit of mTOR Complex 1 (mTORC1) and 2 (mTORC2)[110]. These complexes regulate cell growth by modulating protein synthesis, autophagy, and other metabolic pathways[110]. The mTORC1 and mTORC2 complexes are downstream effectors of the PI3K/AKT/MTOR signaling pathway and facilitate integration of the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK signaling pathways[111,112,113].

Alterations and prevalence: Recurrent activating mutations differentially activate mTORC1 or mTORC2 leading to either S6K1/4EBP1 or AKT1 phosphorylation, respectively[114]. Somatic mutations in MTOR are observed in 12% of uterine corpus endometrial carcinoma and skin cutaneous melanoma, 8% of kidney renal clear cell carcinoma and colorectal adenocarcinoma, 7% of stomach adenocarcinoma, 5% of lung adenocarcinoma, 4% of esophageal adenocarcinoma and lung squamous cell carcinoma, 3% of bladder urothelial carcinoma, kidney chromophobe, and cervical squamous cell carcinoma, and 2% of liver hepatocellular carcinoma, ovarian serous cystadenocarcinoma, breast invasive carcinoma, head and neck squamous cell carcinoma, pancreatic adenocarcinoma, thymoma, glioblastoma multiforme, and acute myeloid leukemia[15,16]. MTOR amplification is observed in 2% of ovarian serous cystadenocarcinoma, sarcoma, and esophageal adenocarcinoma[15,16]. Alterations in MTOR are also observed in pediatric cancers[16].

Biomarker Descriptions (continued)

Somatic mutations are observed in 12% of non-Hodgkin lymphoma (2 in 17 cases), 7% of Hodgkin lymphoma (4 in 61 cases), 5% of soft tissue sarcoma (2 in 38 cases) and T-lymphoblastic leukemia/lymphoma (2 in 41 cases), 1% of B-lymphoblastic leukemia/lymphoma (3 in 252 cases) and bone cancer (3 in 327 cases), and less than 1% of embryonal tumors (3 in 332 cases), glioma (1 in 297 cases), leukemia (1 in 311 cases), and Wilms tumor (1 in 710 cases)[16]. Amplification of MTOR is observed in less than 1% of leukemia (2 in 250 cases) and B-lymphoblastic leukemia/lymphoma (5 in 731 cases)[16].

Potential relevance: Two first generation MTOR inhibitors termed rapalogs (analogues of rapamycin) have been approved by the FDA: temsirolimus[115] (2007) for the treatment of renal cell carcinoma (RCC) and everolimus[116] (2009) for the treatment of breast, pancreatic, gastrointestinal, and lung cancers, RCC, and subependymal giant cell astrocytomas. Mutations in the FRB domain of mTOR are a potential mechanism of acquired resistance to first generation rapalogs[112,117]. While first-generation rapalogs form inhibitory complexes with FKBP-12, second generation mTOR inhibitors such as PF-04691502 and gedatolisib target the mTOR kinase domain directly[118].

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[119]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[120,121]. 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[122]. 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[123]. 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)[123]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[124,125,126,127,128]. 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[121]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[120,121,125,129].

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[120,121,130,131]. 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[130,131].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[132] (2014) and nivolumab[133] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[132] 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[132]. Dostarlimab[134] (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[126,135]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[136] (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[126,137,138]. 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[138]. 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[139,140]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[139,140].

USP9X p.(D134Afs*8) c.401_406delATGAAGinsC

ubiquitin specific peptidase 9 X-linked

Background: The USP9X gene encodes the ubiquitin specific peptidase 9 X-linked protein[21]. USP9X is a deubiquitinating enzyme (DUB) and a member of the ubiquitin-specific protease (USP) subclass of cysteine proteases[27]. DUBs catalyze the removal of ubiquitin from target proteins, thereby counter-regulating post-translational ubiquitin modifications within the cell[27,28]. USP9X has many substrates and is commonly upregulated in several solid tumor types, supporting an oncogenic role for USP9X[28]. Conversely, in some cancer types, USP9X has been observed to function as a tumor suppressor, suggesting its exact role in cancer may be dependent on its substrates[28]. In breast cancer, USP9X has been shown to stabilize BRCA1 by inhibiting its ubiquitination, thereby influencing the regulation of homologous recombination and repair[28].

Alterations and prevalence: Somatic mutations are observed in 16% of uterine corpus endometrial carcinoma, 11% of skin cutaneous melanoma, 7% of colorectal adenocarcinoma, 6% of cholangiocarcinoma, and 5% of stomach adenocarcinoma, lung squamous cell

Biomarker Descriptions (continued)

carcinoma, diffuse large B-cell lymphoma (DLBCL), and head and neck squamous cell carcinoma[15,16]. Biallelic deletion in USP9X is observed in 4% of esophageal adenocarcinoma, 3% of head and neck squamous cell carcinoma, and 2% of mesothelioma, uterine carcinosarcoma, and lung squamous cell carcinoma[15,16]. Alterations in USP9X are also observed in the pediatric population[16]. Somatic mutations are observed in 2% of Hodgkin lymphoma (1 in 61 cases) and bone cancer (5 in 327 cases) and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases), glioma (2 in 297 cases), and leukemia (1 in 311 cases)[16]. Biallelic deletion in USP9X is observed in less than 1% of leukemia (2 in 250 cases) and B-lymphoblastic leukemia/lymphoma (2 in 731 cases)[16].

Potential relevance: Currently, no therapies are approved for USP9X aberrations.

SPEN deletion

spen family transcriptional repressor

Background: SPEN encodes spen family transcriptional repressor[21]. SPEN plays a role in chromosome X inactivation and regulation of transcription[40,41,42]. As a transcriptional repressor, SPEN sequesters transcriptional activators and interacts with other repressors and chromatin remodeling complexes, such as histone deacetylases (HDACs) and the NuRD complex[40,42]. In ERα-positive breast cancers, SPEN binds ERα in a ligand-independent manner and negatively regulates the transcription of ERα targets, acting as a tumor suppressor gene to regulate cell proliferation, tumor growth, and survival[43,44].

Alterations and prevalence: Somatic mutations in SPEN are observed in 13% of skin cutaneous melanoma, 12% of uterine corpus endometrial carcinoma, 10% of stomach adenocarcinoma, 7% of diffuse large B-cell lymphoma, bladder urothelial carcinoma, and colorectal adenocarcinoma, 6% of cervical squamous cell carcinoma, 5% of head and neck squamous cell carcinoma and lung adenocarcinoma, 4% of lung squamous cell carcinoma and ovarian serous cystadenocarcinoma, 3% of kidney renal clear cell carcinoma, kidney renal papillary cell carcinoma, breast invasive carcinoma, glioblastoma multiforme, and acute myeloid leukemia, and 2% of pancreatic adenocarcinoma, adrenocortical carcinoma, liver hepatocellular carcinoma, uterine carcinosarcoma, and esophageal adenocarcinoma[15,16]. Biallelic loss of SPEN is observed in 6% of cholangiocarcinoma and 2% of pheochromocytoma and paraganglioma[15,16].

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

EPHA2 deletion

EPH receptor A2

Background: The EPHA2 gene encodes the EPH receptor A2[21]. EPHA2 is a member of the erythropoietin-producing hepatocellular carcinoma (Eph) receptors, a group of receptor tyrosine kinases divided into EPHA (EphA1-10) and EPHB (EphB1-6) classes of proteins[32,33]. Like classical tyrosine kinase receptors, Eph activation is initiated by ligand binding resulting downstream signaling involved in various cellular processes including cell growth, differentiation, and apoptosis[33]. Specifically, Eph-EphrinA ligand interaction regulates pathways critical for malignant transformation and key downstream target proteins including PI3K, SRC, Rho and Rac1 GTPases, MAPK, and integrins[32,33].

Alterations and prevalence: Somatic mutations in EPHA2 are observed in 11% of cholangiocarcinoma, 7% of uterine corpus endometrial carcinoma, stomach adenocarcinoma, and skin cutaneous melanoma, 6% of bladder urothelial carcinoma, and 5% of diffuse large B-cell lymphoma (DLBCL) and cervical squamous cell carcinoma[15,16].

Potential relevance: Currently, no therapies are approved for EPHA2 aberrations.

HLA-B deletion

major histocompatibility complex, class I, B

Background: The HLA-B gene encodes the major histocompatibility complex, class I, B[21]. 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[45]. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M[46]. 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[47,48,49]. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B[50].

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[15,16]. Biallelic loss of HLA-B is observed in 5% of DLBCL[15,16].

Biomarker Descriptions (continued)

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

MTAP::CDKN2B-AS1-004 fusion

methylthioadenosine phosphorylase

Background: The MTAP gene encodes methylthioadenosine phosphorylase[21]. 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[29,30]. Loss of MTAP function is commonly observed in cancer due to deletion or promotor methylation which results in the loss of MTA phosphorylation and sensitivity of MTAP-deficient cells to purine synthesis inhibitors and to methionine deprivation[30].

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[30,31]. 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[15,16]. Somatic mutations in MTAP have been found in 3% of uterine corpus endometrial carcinoma[15,16].

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

CTCF deletion

CCCTC-binding factor

Background: The CTCF gene encodes the CCCTC-binding factor, a member of the BORIS + CTCF gene family[21]. CTCF promotes the formation of cohesion-mediated loops, the formation of which organizes chromatin into self-interacting topologically associated domains (TADs) and influences gene expression[51]. Additionally, CTCF has been observed to function as a transcription factor through the binding of transcriptional start sites (TSS), but may also play a role in transcriptional repression[51,52,53]. CTCF mutations lead to disruption of TAD boundaries which alters gene expression and may promote oncogenesis[51].

Alterations and prevalence: Somatic mutations in CTCF are observed in 25% of uterine corpus endometrial carcinoma, 5% of stomach adenocarcinoma and uterine carcinosarcoma, 4% of colorectal adenocarcinoma, and 3% of bladder urothelial carcinoma, head and neck squamous cell carcinoma, and cholangiocarcinoma[15,16].

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

CDH1 deletion

cadherin 1

Background: The CDH1 gene encodes epithelial cadherin or E-cadherin, a member of the cadherin superfamily that includes the classical cadherins: neural cadherin (N-cadherin), retinal cadherin (R-cadherin), and placental cadherin (P-cadherin)[21,54]. E-cadherin proteins, composed of 5 extracellular cadherin repeats, a single transmembrane domain, and conserved cytoplasmic tail, are calcium-dependent transmembrane glycoproteins expressed in epithelial cells[21]. Extracellular E-cadherin monomers form homodimers with those on adjacent cells to form adherens junctions. Adherens junctions are reinforced by intracellular complexes formed between the cytoplasmic tail of E-cadherin and catenins, proteins which directly anchor cadherins to actin filaments[55]. E-cadherin is a critical tumor suppressor and when lost, results in epithelial-mesenchymal transition (EMT), anchorage-independent cell growth, loss of cell polarity, and tumor metastasis[56,57]. Germline mutations in CDH1 are enriched in a rare autosomal-dominant genetic malignancies such as hereditary diffuse gastric cancer, lobular breast cancer, and colorectal cancer[58].

Alterations and prevalence: Mutations in CDH1 are predominantly missense or truncating and have been observed to result in loss of function[15,16,59,60]. In cancer, somatic mutation of CDH1 is observed in 12% of invasive breast carcinoma, 10% of stomach adenocarcinoma, 7% of uterine corpus endometrial carcinoma, 4% of colorectal adenocarcinoma and skin cutaneous melanoma, 3% of bladder urothelial carcinomas, and 2% of lung squamous cell and liver hepatocelluar carcinomas[15,16]. Biallelic deletion of CDH1 is observed in 3% of prostate adenocarcinoma and ovarian serous cystadenocarcinoma, and 2% of esophageal adenocarcinoma, diffuse large B-cell lymphoma, and breast invasive carcinoma[15,16].

Potential relevance: Currently, no therapies are approved for CDH1 aberrations.

Biomarker Descriptions (continued)

ZFHX3 deletion

zinc finger homeobox 3

Background: ZFHX3 encodes zinc finger homeobox 3, a large transcription factor composed of several DNA binding domains, including seventeen zinc finger domains and four homeodomains[21,100,101]. Functionally, ZFHX3 is found to be necessary for neuronal and myogenic differentiation[101,102]. ZFHX3 is capable of binding and repressing transcription of α-fetoprotein (AFP), thereby negatively regulating the expression of MYB and cancer cell growth[103,104,105,106,107]. In addition, ZFHX3 has been observed to be altered in several cancer types, supporting a tumor suppressor role for ZFHX3[103,106,108,109].

Alterations and prevalence: Somatic mutations in ZFHX3 are observed in 24% of uterine corpus endometrial carcinoma, 14% of skin cutaneous melanoma, 10% of colorectal adenocarcinoma, 9% of stomach adenocarcinoma, 8% of lung squamous cell carcinoma, 6% of cervical squamous cell carcinoma, 5% of uterine carcinosarcoma, bladder urothelial carcinoma, and lung adenocarcinoma, 3% of head and neck squamous cell carcinoma, adrenocortical carcinoma, cholangiocarcinoma, esophageal adenocarcinoma, and prostate adenocarcinoma, and 2% of diffuse large B-cell lymphoma, glioblastoma multiforme, pancreatic adenocarcinoma, liver hepatocellular carcinoma, thyroid carcinoma, breast invasive carcinoma, ovarian serous cystadenocarcinoma, thymoma, sarcoma, and acute myeloid leukemia[15,16]. Biallelic loss of ZFHX3 is observed in 6% of prostate adenocarcinoma, 4% of uterine carcinosarcoma, 3% of ovarian serous cystadenocarcinoma, and 2% of uterine corpus endometrial carcinoma, breast invasive carcinoma, and esophageal adenocarcinoma[15,16].

Potential relevance: Currently, no therapies are approved for ZFHX3 aberrations.

CYP2D6 c.506-1G>A

cytochrome P450 family 2 subfamily D member 6

Background: The CYP2D6 gene encodes cytochrome P450 family 2 subfamily D member 6, a member of the cytochrome P450 superfamily of proteins[21]. The cytochrome P450 proteins are monooxygenases that play important roles in the biotransformation of xenobiotics and carcinogens, and the synthesis of cholesterol, steroids and other lipids[21,22]. CYP2D6 is a key enzyme involved in the biotransformation of the prodrug tamoxifen to its active metabolites, endoxifen and 4-hydroxytamoxifen[23,24]. The CYP2D6 gene is highly polymorphic, and inherited CYP2D6 polymorphisms in individuals may result in absent, reduced, normal, or high CYP2D6 enzyme activity leading to poor, intermediate, normal, or ultrarapid metabolism of tamoxifen[23,24,25,26]. CYP2D6 genotype may impact response to tamoxifen treatment and clinical outcomes[25].

Alterations and prevalence: Somatic mutations in CYP2D6 are observed in 4% of uterine corpus endometrial carcinoma, 3% of stomach adenocarcinoma and cholangiocarcinoma, and 2% of colorectal adenocarcinoma, skin cutaneous melanoma, and kidney chromophobe[15,16]. Biallelic loss of CYP2D6 is observed in 2% of ovarian serous cystadenocarcinoma[15,16]. Amplification of CYP2D6 is observed in 4% of skin cutaneous melanoma, 3% of cholangiocarcinoma, and 2% of pancreatic adenocarcinoma[15,16].

Potential relevance: Currently, no therapies are approved for CYP2D6.

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 (continued)

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

Relevant Therapy Summary

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

AKT1 p.(E17K) c.49G>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
capivasertib + fulvestrant	○	○	○	✖	✖
ipatasertib + chemotherapy	✖	✖	✖	✖	● (II)
ipatasertib, chemotherapy	✖	✖	✖	✖	● (II)
HTL-0039732, atezolizumab	✖	✖	✖	✖	● (I/II)
inavolisib, hormone therapy	✖	✖	✖	✖	● (I/II)
ALTA-2618	✖	✖	✖	✖	● (I)
ATV-1601	✖	✖	✖	✖	● (I)
IPN-60090, capivasertib	✖	✖	✖	✖	● (I)

ARID1A deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
pamiparib, tislelizumab	✖	✖	✖	✖	● (II)
tucidinostat, catequentinib, PD-1 Inhibitor, anti-PD-L1 antibody	✖	✖	✖	✖	● (II)

CTNNB1 p.(T41I) c.122C>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
tegatrabetan	✖	✖	✖	✖	● (I/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	***1.51%***
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 (6.2.4 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.

References

1. Valenta et al. The many faces and functions of β-catenin. EMBO J. 2012 Jun 13;31(12):2714-36. PMID: 22617422
2. Korinek et al. Constitutive transcriptional activation by a beta-catenin-Tcf complex in APC-/- colon carcinoma. Science. 1997 Mar 21;275(5307):1784-7. PMID: 9065401
3. Aberle et al. beta-catenin is a target for the ubiquitin-proteasome pathway. EMBO J. 1997 Jul 1;16(13):3797-804. PMID: 9233789
4. Winston et al. The SCFbeta-TRCP-ubiquitin ligase complex associates specifically with phosphorylated destruction motifs in IkappaBalpha and beta-catenin and stimulates IkappaBalpha ubiquitination in vitro. Genes Dev. 1999 Feb 1;13(3):270-83. PMID: 9990852
5. Kitagawa et al. An F-box protein, FWD1, mediates ubiquitin-dependent proteolysis of beta-catenin. EMBO J. 1999 May 4;18(9):2401-10. PMID: 10228155
6. Gao et al. Exon 3 mutations of CTNNB1 drive tumorigenesis: a review. Oncotarget. 2018 Jan 12;9(4):5492-5508. PMID: 29435196
7. Liu et al. Control of beta-catenin phosphorylation/degradation by a dual-kinase mechanism. Cell. 2002 Mar 22;108(6):837-47. PMID: 11955436
8. Miyoshi et al. Activation of the beta-catenin gene in primary hepatocellular carcinomas by somatic alterations involving exon 3. Cancer Res. 1998 Jun 15;58(12):2524-7. PMID: 9635572
9. Morin et al. Activation of beta-catenin-Tcf signaling in colon cancer by mutations in beta-catenin or APC. Science. 1997 Mar 21;275(5307):1787-90. PMID: 9065402
10. Schulze et al. Exome sequencing of hepatocellular carcinomas identifies new mutational signatures and potential therapeutic targets. Nat. Genet. 2015 May;47(5):505-511. PMID: 25822088
11. Ahn et al. Genomic portrait of resectable hepatocellular carcinomas: implications of RB1 and FGF19 aberrations for patient stratification. Hepatology. 2014 Dec;60(6):1972-82. PMID: 24798001
12. Harding et al. Prospective Genotyping of Hepatocellular Carcinoma: Clinical Implications of Next-Generation Sequencing for Matching Patients to Targeted and Immune Therapies. Clin. Cancer Res. 2018 Oct 29. PMID: 30373752
13. Cancer Genome Atlas Research et al. Integrated genomic characterization of endometrial carcinoma. Nature. 2013 May 2;497(7447):67-73. PMID: 23636398
14. Soumerai et al. Clinical Utility of Prospective Molecular Characterization in Advanced Endometrial Cancer. Clin. Cancer Res. 2018 Dec 1;24(23):5939-5947. PMID: 30068706
15. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. Nat. Genet. 2013 Oct;45(10):1113-20. PMID: 24071849
16. 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
17. Blakely et al. Evolution and clinical impact of co-occurring genetic alterations in advanced-stage EGFR-mutant lung cancers. Nat. Genet. 2017 Dec;49(12):1693-1704. PMID: 29106415
18. NCCN Guidelines® - NCCN-Soft Tissue Sarcoma [Version 1.2025]
19. Moreno et al. High frequency of WNT-activated medulloblastomas with CTNNB1 wild type suggests a higher proportion of hereditary cases in a Latin-Iberian population. Front Oncol. 2023;13:1237170. PMID: 37746264
20. 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
21. 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
22. Schmelzle et al. Esophageal cancer proliferation is mediated by cytochrome P450 2C9 (CYP2C9). Prostaglandins Other Lipid Mediat. 2011 Feb;94(1-2):25-33. PMID: 21167292
23. Brooks et al. CYP2D6 phenotype, tamoxifen, and risk of contralateral breast cancer in the WECARE Study. Breast Cancer Res. 2018 Dec 10;20(1):149. PMID: 30526633
24. Dezentjé et al. Clinical implications of CYP2D6 genotyping in tamoxifen treatment for breast cancer. Clin Cancer Res. 2009 Jan 1;15(1):15-21. PMID: 19118028
25. He et al. CYP2D6 Genotype Predicts Tamoxifen Discontinuation and Prognosis in Patients With Breast Cancer. J Clin Oncol. 2020 Feb 20;38(6):548-557. PMID: 31800347
26. Hertz et al. In vivo assessment of the metabolic activity of CYP2D6 diplotypes and alleles. Br J Clin Pharmacol. 2015 Nov;80(5):1122-30. PMID: 25907378
27. Dufner et al. Ubiquitin-specific protease 8 (USP8/UBPy): a prototypic multidomain deubiquitinating enzyme with pleiotropic functions. Biochem Soc Trans. 2019 Dec 20;47(6):1867-1879. PMID: 31845722

References (continued)

28. Lu et al. USP9X stabilizes BRCA1 and confers resistance to DNA-damaging agents in human cancer cells. Cancer Med. 2019 Nov;8(15):6730-6740. PMID: 31512408
29. Harasawa et al. Chemotherapy targeting methylthioadenosine phosphorylase (MTAP) deficiency in adult T cell leukemia (ATL). Leukemia. 2002 Sep;16(9):1799-807. PMID: 12200696
30. 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
31. Katya et al. Cancer Dependencies: PRMT5 and MAT2A in MTAP/p16-Deleted Cancers. 10.1146/annurev-cancerbio-030419-033444
32. Tan et al. EPHA2 mutations with oncogenic characteristics in squamous cell lung cancer and malignant pleural mesothelioma. Oncogenesis. 2019 Sep 4;8(9):49. PMID: 31484920
33. Tandon et al. Emerging strategies for EphA2 receptor targeting for cancer therapeutics. Expert Opin Ther Targets. 2011 Jan;15(1):31-51. PMID: 21142802
34. Wu et al. ARID1A mutations in cancer: another epigenetic tumor suppressor?. Cancer Discov. 2013 Jan;3(1):35-43. PMID: 23208470
35. Wilson et al. SWI/SNF nucleosome remodellers and cancer. Nat. Rev. Cancer. 2011 Jun 9;11(7):481-92. PMID: 21654818
36. Alver et al. The SWI/SNF Chromatin Remodelling Complex Is Required for Maintenance of Lineage Specific Enhancers. Nat Commun. 8;14648. PMID: 28262751
37. Mehrvarz Sarshekeh et al. ARID1A Mutation May Define an Immunologically Active Subgroup in Patients with Microsatellite Stable Colorectal Cancer. Clin Cancer Res. 2021 Mar 15;27(6):1663-1670. PMID: 33414133
38. https://nuvectis.com/press-release-view/?i=114174
39. https://www.morphosys.com/en/news/morphosys-receives-us-fda-fast-track-designation-tulmimetostat-endometrial-cancer
40. Dossin et al. SPEN integrates transcriptional and epigenetic control of X-inactivation. Nature. 2020 Feb;578(7795):455-460. PMID: 32025035
41. Li et al. SPEN induces miR-4652-3p to target HIPK2 in nasopharyngeal carcinoma. Cell Death Dis. 2020 Jul 2;11(7):509. PMID: 32641685
42. Radio et al. SPEN haploinsufficiency causes a neurodevelopmental disorder overlapping proximal 1p36 deletion syndrome with an episignature of X chromosomes in females. Am J Hum Genet. 2021 Mar 4;108(3):502-516. PMID: 33596411
43. Légaré et al. The Estrogen Receptor Cofactor SPEN Functions as a Tumor Suppressor and Candidate Biomarker of Drug Responsiveness in Hormone-Dependent Breast Cancers. Cancer Res. 2015 Oct 15;75(20):4351-63. PMID: 26297734
44. Légaré et al. SPEN, a new player in primary cilia formation and cell migration in breast cancer. Breast Cancer Res. 2017 Sep 6;19(1):104. PMID: 28877752
45. Hulpke et al. The MHC I loading complex: a multitasking machinery in adaptive immunity. Trends Biochem Sci. PMID: 23849087
46. 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
47. Rossjohn et al. T cell antigen receptor recognition of antigen-presenting molecules. Annu Rev Immunol. 2015;33:169-200. PMID: 25493333
48. Parham. MHC class I molecules and KIRs in human history, health and survival. Nat Rev Immunol. 2005 Mar;5(3):201-14. PMID: 15719024
49. Sidney et al. HLA class I supertypes: a revised and updated classification. BMC Immunol. 2008 Jan 22;9:1. PMID: 18211710
50. 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
51. Debaugny et al. CTCF and CTCFL in cancer. Curr Opin Genet Dev. 2020 Apr;61:44-52. PMID: 32334335
52. Lutz et al. Transcriptional repression by the insulator protein CTCF involves histone deacetylases. Nucleic Acids Res. 2000 Apr 15;28(8):1707-13. PMID: 10734189
53. Holwerda et al. CTCF: the protein, the binding partners, the binding sites and their chromatin loops. Philos Trans R Soc Lond B Biol Sci. 2013;368(1620):20120369. PMID: 23650640
54. Halbleib et al. Cadherins in development: cell adhesion, sorting, and tissue morphogenesis. Genes Dev. 2006 Dec 1;20(23):3199-214. PMID: 17158740
55. Pećina-Slaus. Tumor suppressor gene E-cadherin and its role in normal and malignant cells. Cancer Cell Int. 2003 Oct 14;3(1):17. PMID: 14613514

References (continued)

56. Hirohashi. Inactivation of the E-cadherin-mediated cell adhesion system in human cancers. Am J Pathol. 1998 Aug;153(2):333-9. PMID: 9708792
57. Bruner et al. Loss of E-Cadherin-Dependent Cell-Cell Adhesion and the Development and Progression of Cancer. Cold Spring Harb Perspect Biol. 2018 Mar 1;10(3). PMID: 28507022
58. Adib et al. CDH1 germline variants are enriched in patients with colorectal cancer, gastric cancer, and breast cancer. Br J Cancer. 2022 Mar;126(5):797-803. PMID: 34949788
59. Al-Ahmadie et al. Frequent somatic CDH1 loss-of-function mutations in plasmacytoid variant bladder cancer. Nat Genet. 2016 Apr;48(4):356-8. PMID: 26901067
60. Kim et al. Loss of CDH1 (E-cadherin) expression is associated with infiltrative tumour growth and lymph node metastasis. Br J Cancer. 2016 Jan 19;114(2):199-206. PMID: 26742007
61. Gonzalez et al. The Akt kinases: isoform specificity in metabolism and cancer. Cell Cycle. 2009 Aug 15;8(16):2502-8. PMID: 19597332
62. Porta et al. Targeting PI3K/Akt/mTOR Signaling in Cancer. Front Oncol. 2014 Apr 14;4:64. doi: 10.3389/fonc.2014.00064. eCollection 2014. PMID: 24782981
63. Mundi et al. AKT in cancer: new molecular insights and advances in drug development. Br J Clin Pharmacol. 2016 Oct;82(4):943-56. PMID: 27232857
64. Carpten et al. A transforming mutation in the pleckstrin homology domain of AKT1 in cancer. Nature. 2007 Jul 26;448(7152):439-44. Epub 2007 Jul 4. PMID: 17611497
65. Shoji et al. The oncogenic mutation in the pleckstrin homology domain of AKT1 in endometrial carcinomas. Br. J. Cancer. 2009 Jul 7;101(1):145-8. PMID: 19491896
66. Parikh et al. Disruption of PH-kinase domain interactions leads to oncogenic activation of AKT in human cancers. Proc. Natl. Acad. Sci. U.S.A. 2012 Nov 20;109(47):19368-73. PMID: 23134728
67. American Association for Cancer Research. Capivasertib Active against AKT1-Mutated Cancers. Cancer Discov. 2018 Nov 14. PMID: 30429128
68. Hyman et al. AKT Inhibition in Solid Tumors With AKT1 Mutations. J. Clin. Oncol. 2017 Jul 10;35(20):2251-2259. PMID: 28489509
69. Paterni et al. Estrogen receptors alpha (ERα) and beta (ERβ): subtype-selective ligands and clinical potential. Steroids. 2014 Nov;90:13-29. PMID: 24971815
70. Dahlman-Wright et al. International Union of Pharmacology. LXIV. Estrogen receptors. Pharmacol. Rev. 2006 Dec;58(4):773-81. PMID: 17132854
71. Marino et al. Estrogen signaling multiple pathways to impact gene transcription. Curr. Genomics. 2006;7(8):497-508. PMID: 18369406
72. Lovén et al. MYCN-regulated microRNAs repress estrogen receptor-alpha (ESR1) expression and neuronal differentiation in human neuroblastoma. Proc Natl Acad Sci U S A. 2010 Jan 26;107(4):1553-8. PMID: 20080637
73. Cao et al. Estrogen receptor α enhances the transcriptional activity of ETS-1 and promotes the proliferation, migration and invasion of neuroblastoma cell in a ligand dependent manner. BMC Cancer. 2015 Jun 30;15:491. PMID: 26122040
74. Chang. Tamoxifen resistance in breast cancer. Biomol Ther (Seoul). 2012 May;20(3):256-67. PMID: 24130921
75. Toy et al. ESR1 ligand-binding domain mutations in hormone-resistant breast cancer. Nat. Genet. 2013 Dec;45(12):1439-45. PMID: 24185512
76. Jeselsohn et al. Emergence of Constitutively Active Estrogen Receptor-α Mutations in Pretreated Advanced Estrogen Receptor-Positive Breast Cancer. Clin. Cancer Res. 2014 Apr 1;20(7):1757-1767. PMID: 24398047
77. Robinson et al. Activating ESR1 mutations in hormone-resistant metastatic breast cancer. Nat Genet. 2013 Dec;45(12):1446-51. doi: 10.1038/ng.2823. Epub 2013 Nov 3. PMID: 24185510
78. Hartmaier et al. Recurrent hyperactive ESR1 fusion proteins in endocrine therapy-resistant breast cancer. Ann. Oncol. 2018 Apr 1;29(4):872-880. PMID: 29360925
79. Matissek et al. Expressed Gene Fusions as Frequent Drivers of Poor Outcomes in Hormone Receptor-Positive Breast Cancer. Cancer Discov. 2018 Mar;8(3):336-353. PMID: 29242214
80. Lei et al. ESR1 fusions drive endocrine therapy resistance and metastasis in breast cancer. Mol Cell Oncol. 2018;5(6):e1526005. PMID: 30525098
81. Lei et al. Functional Annotation of ESR1 Gene Fusions in Estrogen Receptor-Positive Breast Cancer. Cell Rep. 2018 Aug 7;24(6):1434-1444.e7. PMID: 30089255
82. Basudan et al. Frequent ESR1 and CDK Pathway Copy-Number Alterations in Metastatic Breast Cancer. Mol. Cancer Res. 2019 Feb;17(2):457-468. PMID: 30355675

References (continued)

83. De Braekeleer et al. ETV6 fusion genes in hematological malignancies: a review. Leuk. Res. 2012 Aug;36(8):945-61. PMID: 22578774
84. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217639Orig1s001lbl.pdf
85. NCCN Guidelines® - NCCN-Breast Cancer [Version 5.2025]
86. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/218881s000lbl.pdf
87. https://www.accutarbio.com/accutar-biotechnology-receives-fda-fast-track-designation-for-ac699-in-er-her2-breast-cancer/
88. https://sermonixpharma.com/sermonix-receives-fda-fast-track-designation-for-investigational-drug-lasofoxifene/
89. https://www.astrazeneca.com/content/dam/az/PDF/2022/h1-2022/H1-2022-results-announcement.pdf
90. https://www.businesswire.com/news/home/20160106006206/en/Innocrin-Pharmaceuticals-Granted-Fast-Track-Designation-FDA
91. https://www.accessdata.fda.gov/drugsatfda_docs/label/2002/17970s37s44s49lbl.pdf
92. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021344s044lbl.pdf
93. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/020726s043lbl.pdf
94. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/020753s025lbl.pdf
95. Tamoxifen--an update on current data and where it can now be used. Breast Cancer Res. Treat. 2002 Oct;75 Suppl 1:S7-12; discussion S33-5. PMID: 12353826
96. Kim et al. Estrogen receptor (ESR1) mRNA expression and benefit from tamoxifen in the treatment and prevention of estrogen receptor-positive breast cancer. J. Clin. Oncol. 2011 Nov 1;29(31):4160-7. PMID: 21947828
97. Jeselsohn et al. ESR1 mutations—a mechanism for acquired endocrine resistance in breast cancer. Nat Rev Clin Oncol. 2015 Oct;12(10):573-83. PMID: 26122181
98. Angus et al. ESR1 mutations: Moving towards guiding treatment decision-making in metastatic breast cancer patients. Cancer Treat. Rev. 2017 Jan;52:33-40. PMID: 27886589
99. Reinert et al. Clinical Implications of ESR1 Mutations in Hormone Receptor-Positive Advanced Breast Cancer. Front Oncol. 2017 Mar 15;7:26. PMID: 28361033
100. Zhao et al. Zinc Finger Homeodomain Factor Zfhx3 Is Essential for Mammary Lactogenic Differentiation by Maintaining Prolactin Signaling Activity. J Biol Chem. 2016 Jun 10;291(24):12809-12820. PMID: 27129249
101. Miura et al. Cloning and characterization of an ATBF1 isoform that expresses in a neuronal differentiation-dependent manner. J Biol Chem. 1995 Nov 10;270(45):26840-8. PMID: 7592926
102. Berry et al. Positive and negative regulation of myogenic differentiation of C2C12 cells by isoforms of the multiple homeodomain zinc finger transcription factor ATBF1. J Biol Chem. 2001 Jul 6;276(27):25057-65. PMID: 11312261
103. Kataoka et al. Alpha-fetoprotein producing gastric cancer lacks transcription factor ATBF1. Oncogene. 2001 Feb 15;20(7):869-73. PMID: 11314020
104. Ninomiya et al. Regulation of the alpha-fetoprotein gene by the isoforms of ATBF1 transcription factor in human hepatoma. Hepatology. 2002 Jan;35(1):82-7. PMID: 11786962
105. Kaspar et al. Myb-interacting protein, ATBF1, represses transcriptional activity of Myb oncoprotein. J Biol Chem. 1999 May 14;274(20):14422-8. PMID: 10318867
106. Sun et al. Frequent somatic mutations of the transcription factor ATBF1 in human prostate cancer. Nat Genet. 2005 Apr;37(4):407-12. PMID: 15750593
107. Mabuchi et al. Tumor suppressor, AT motif binding factor 1 (ATBF1), translocates to the nucleus with runt domain transcription factor 3 (RUNX3) in response to TGF-beta signal transduction. Biochem Biophys Res Commun. 2010 Jul 23;398(2):321-5. PMID: 20599712
108. Sun et al. Deletion of atbf1/zfhx3 in mouse prostate causes neoplastic lesions, likely by attenuation of membrane and secretory proteins and multiple signaling pathways. Neoplasia. 2014 May;16(5):377-89. PMID: 24934715
109. Kawaguchi et al. A diagnostic marker for superficial urothelial bladder carcinoma: lack of nuclear ATBF1 (ZFHX3) by immunohistochemistry suggests malignant progression. BMC Cancer. 2016 Oct 18;16(1):805. PMID: 27756245
110. Saxton et al. mTOR Signaling in Growth, Metabolism, and Disease. Cell. 2017 Mar 9;168(6):960-976. PMID: 28283069
111. Pópulo et al. The mTOR signalling pathway in human cancer. Int J Mol Sci. 2012;13(2):1886-918. PMID: 22408430
112. Faes et al. Resistance to mTORC1 Inhibitors in Cancer Therapy: From Kinase Mutations to Intratumoral Heterogeneity of Kinase Activity. Oxid Med Cell Longev. 2017;2017:1726078. Epub 2017 Feb 9. PMID: 28280521

References (continued)

113. Mendoza et al. The Ras-ERK and PI3K-mTOR pathways: cross-talk and compensation. Trends Biochem. Sci. 2011 Jun;36(6):320-8. PMID: 21531565
114. Grabiner et al. A diverse array of cancer-associated MTOR mutations are hyperactivating and can predict rapamycin sensitivity. Cancer Discov. 2014 May;4(5):554-63. PMID: 24631838
115. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022088s021s023lbl.pdf
116. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/203985s023,022334s051lbl.pdf
117. Rodrik-Outmezguine et al. Overcoming mTOR resistance mutations with a new-generation mTOR inhibitor. Nature. 2016 Jun 9;534(7606):272-6. PMID: 27279227
118. Del Campo et al. A randomized phase II non-comparative study of PF-04691502 and gedatolisib (PF-05212384) in patients with recurrent endometrial cancer. Gynecol. Oncol. 2016 Jul;142(1):62-69. PMID: 27103175
119. Lander et al. Initial sequencing and analysis of the human genome. Nature. 2001 Feb 15;409(6822):860-921. PMID: 11237011
120. 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
121. Nojadeh et al. Microsatellite instability in colorectal cancer. EXCLI J. 2018;17:159-168. PMID: 29743854
122. 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
123. 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
124. 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
125. Imai et al. Carcinogenesis and microsatellite instability: the interrelationship between genetics and epigenetics. Carcinogenesis. 2008 Apr;29(4):673-80. PMID: 17942460
126. NCCN Guidelines® - NCCN-Colon Cancer [Version 5.2025]
127. Pawlik et al. Colorectal carcinogenesis: MSI-H versus MSI-L. Dis. Markers. 2004;20(4-5):199-206. PMID: 15528785
128. 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
129. 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
130. 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
131. Bonneville et al. Landscape of Microsatellite Instability Across 39 Cancer Types. JCO Precis Oncol. 2017;2017. PMID: 29850653
132. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125514s178lbl.pdf
133. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125554s131lbl.pdf
134. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761174s009lbl.pdf
135. NCCN Guidelines® - NCCN-Rectal Cancer [Version 4.2025]
136. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/125377s136lbl.pdf
137. 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
138. 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
139. Hermel et al. The Emerging Role of Checkpoint Inhibition in Microsatellite Stable Colorectal Cancer. J Pers Med. 2019 Jan 16;9(1). PMID: 30654522
140. Ciardiello et al. Immunotherapy of colorectal cancer: Challenges for therapeutic efficacy. Cancer Treat. Rev. 2019 Jun;76:22-32. PMID: 31079031