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Patient Name: 이상희
Gender: M
Sample ID: N25-252

Primary Tumor Site: Lung
Collection Date: 2025.09.22.

Sample Cancer Type: Lung Cancer

Report Highlights

2 Relevant Biomarkers
0 Therapies Available
2 Clinical Trials

Relevant Lung Cancer Findings

Gene	Finding	Gene	Finding
ALK	None detected	NTRK1	None detected
BRAF	None detected	NTRK2	None detected
EGFR	None detected	NTRK3	None detected
ERBB2	None detected	RET	None detected
KRAS	None detected	ROS1	None detected
MET	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	***7.63 Mut/Mb measured***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*ATRX deletion* ATRX, chromatin remodeler Locus: chrX:76763769	None*	None*	1
IIC	*MYCL amplification* MYCL proto-oncogene, bHLH transcription factor Locus: chr1:40362966	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

*BCL6 amplification, CDKN2A p.(R103Vfs*34) c.306_333delGCGGCTGGACGTGCGCGATGCCTGGGGC, KMT2D c.14382+1G>A, Microsatellite stable, NFE2L2 p.(R34G) c.100C>G, NOTCH2 p.(P6Rfs*27) c.17_18delCC, TP53 p.(Y236*) c.708C>G, YAP1 amplification, MPL amplification, MECOM amplification, IL7R amplification, AR amplification, ZMYM3 deletion, Tumor Mutational Burden*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
CDKN2A	p.(R103Vfs*34)	c.306_333delGCGGCTGGACGTGCGCGATGCCTGGGGC	.	chr9:21971024	45.61%	NM_001195132.2	frameshift Deletion
KMT2D	p.(?)	c.14382+1G>A	.	chr12:49422610	61.65%	NM_003482.4	unknown
NFE2L2	p.(R34G)	c.100C>G	COSM132847	chr2:178098945	51.14%	NM_006164.5	missense
NOTCH2	p.(P6Rfs*27)	c.17_18delCC	.	chr1:120612002	21.82%	NM_024408.4	frameshift Deletion
TP53	p.(Y236*)	c.708C>G	.	chr17:7577573	49.37%	NM_000546.6	nonsense
SDHA	p.(S346F)	c.1037C>T	.	chr5:233733	19.25%	NM_004168.4	missense
CTNND2	p.(Q132K)	c.394C>A	.	chr5:11411693	24.40%	NM_001332.4	missense
RAC1	p.(D63N)	c.187G>A	.	chr7:6431634	20.58%	NM_018890.4	missense
OR5L2	p.(S160T)	c.478T>A	.	chr11:55595172	21.12%	NM_001004739.1	missense
SRC	p.(D238N)	c.712G>A	.	chr20:36026110	21.60%	NM_198291.3	missense
SMARCB1	p.(R162K)	c.485G>A	.	chr22:24143253	48.52%	NM_003073.5	missense
KLHL4	p.(V480D)	c.1439T>A	.	chrX:86887324	51.76%	NM_057162.3	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
ATRX	chrX:76763769	0.16	0.53
MYCL	chr1:40362966	7.63	2.44
BCL6	chr3:187440209	4.98	1.76
YAP1	chr11:101981594	5.37	1.86
MPL	chr1:43803495	5.35	1.85
MECOM	chr3:168802636	5.24	1.83
IL7R	chr5:35857035	5.47	1.88
AR	chrX:66766015	7.92	2.51
ZMYM3	chrX:70460753	0.1	0.51
MUTYH	chr1:45794962	5.16	1.81
ADAMTS12	chr5:33527235	5.47	1.88
AMER1	chrX:63409727	5.37	1.86

Biomarker Descriptions

ATRX deletion

ATRX, chromatin remodeler

Background: The ATRX gene encodes the ATRX chromatin remodeler and ATPase/helicase domain protein, which belongs to SWI/SNF family of chromatin remodeling proteins[1]. The SWI/SNF proteins are a group of DNA translocases that use ATP hydrolysis to remodel chromatin structure and maintain genomic integrity by controlling transcriptional regulation, DNA repair, and chromosome stability through the regulation of telomere length[9,10,11,12]. ATRX is a tumor suppressor that interacts with the MRE11-RAD50-NBN (MRN) complex, which is involved in double-stranded DNA (dsDNA) break repair[13,14,15].

Alterations and prevalence: Somatic mutations of ATRX are observed in 38% of brain lower grade glioma, 15% of uterine corpus endometrial carcinoma, 14% of sarcoma, 9% of glioblastoma multiforme and skin cutaneous melanoma, 7% of colorectal adenocarcinoma, 6% of lung adenocarcinoma, stomach adenocarcinoma, and cervical squamous cell carcinoma, 5% of bladder urothelial carcinoma and lung squamous cell carcinoma, 4% of adrenocortical carcinoma, head and neck squamous cell carcinoma and uterine carcinosarcoma, and 2% of diffuse large B-cell lymphoma, ovarian serous cystadenocarcinoma, breast invasive carcinoma, pheochromocytoma and paraganglioma, kidney renal clear cell carcinoma, pancreatic adenocarcinoma, liver hepatocellular carcinoma and kidney chromophobe[6,7]. Biallelic deletion of ATRX is observed in 7% of sarcoma, 3% of kidney chromophobe, and 2% of brain lower grade glioma[6,7]. Although alterations of ATRX in pediatric populations are rare, somatic mutations are observed in 6% of gliomas, 4% of bone cancer, 3% of soft tissue sarcoma, and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 252 cases), embryonal tumor (3 in 332 cases), and leukemia (2 in 354 cases)[7]. Biallelic deletion of ATRX is observed in 1% of peripheral nervous system tumors (1 in 91 cases) in and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases)[7].

Potential relevance: Currently, no therapies are approved for ATRX aberrations. Loss of ATRX protein expression correlates with the presence of ATRX mutations[16,17]. ATRX deficiency along with IDH mutation and TP53 mutation is diagnostic of astrocytoma IDH-mutant as defined by the World Health Organization (WHO)[18,19].

MYCL amplification

MYCL proto-oncogene, bHLH transcription factor

Background: The MYCL gene encodes MYCL proto-oncogene, a basic helix-loop-helix transcription factor[1]. MYCL is a member of MYC oncogene family that includes related transcription factors, MYC and MYCN which regulate transcription in 10-15% of promoter regions[1,87]. MYCL, along with MYC and MYCN, control cell proliferation, replication, evasion of growth suppression and cell death[88].

Alterations and prevalence: Amplification of MYCL was first discovered in small cell lung cancer (SCLC) cell lines and is observed in 8% of ovarian serous cystadenocarcinoma, 6% of bladder urothelial carcinoma and esophageal squamous cell carcinoma, as well as 3% uterine corpus endometrial carcinoma[6,7,89].

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

BCL6 amplification

B-cell CLL/lymphoma 6

Background: The BCL6 gene encodes the B-cell lymphoma 6 (BCL6) transcription repressor, a protein that is responsible for inhibiting the expression of several genes including those involved in the DNA damage response, cell cycle checkpoints, and modulating BCL2 expression[76,77,78]. BCL6 is most commonly expressed in germinal center B-cells and is required for germinal cell formation and affinity maturation during T-cell dependent antibody responses[77]. BCL6 is observed to competitively bind DNA motifs recognized by the oncogenic transcription factor STAT6, thereby repressing STAT6 mediated gene transcription[79,80]. Aberrations in BCL6 often lead to altered target gene transcription, including those involved in cell cycle arrest, differentiation, and apoptosis[76,77].

Alterations and prevalence: BCL6 rearrangement most commonly occurs with immunoglobulin H (IGH) partners and results in the truncation or removal the BCL6 promoter region and juxtaposition of BCL6 downstream of the partner gene promoter[81]. Replacement of the BCL6 promoter resulting from such translocations has been observed to lead to aberrant BCL6 expression[82]. BCL6 rearrangement is a common event in lymphoma and has been observed in up to 40% of diffuse large B-cell lymphoma (DLBCL) and 15% of follicle center lymphomas[77,81]. Somatic mutations in BCL6 are observed in 7% of uterine corpus endometrial carcinoma, 4% of skin cutaneous melanoma, and 3% of stomach adenocarcinoma and colorectal adenocarcinoma, and 2% of uterine carcinosarcoma, lung adenocarcinoma, and sarcoma[6,7]. Mutations in the 5' regulatory sequences of BCL6 are observed in 30-40% of germinal center B-cells and are believed to disrupt BCL6 negative autoregulation[77]. Amplifications are observed in 31% of lung squamous cell carcinoma, 16% of esophageal adenocarcinoma and ovarian serous cystadenocarcinoma, and 14% of head and neck and cervical squamous cell carcinoma, 9% of uterine carcinosarcoma, 6% of uterine corpus endometrial carcinoma, and 2-4% of stomach adenocarcinoma, diffuse large B-cell lymphoma, bladder urothelial carcinoma, breast invasive carcinoma, testicular germ cell tumors, liver hepatocellular carcinoma, and pancreatic adenocarcinoma[6,7]. Alterations in BCL6 are rare in pediatric cancers[6,7]. Somatic mutations in BCL6 are

Biomarker Descriptions (continued)

observed in 3% of soft tissue sarcoma, and less than 1% of bone cancer (3 in 327 cases), embryonal tumors (2 in 332 cases), and glioma (1 in 297 cases)[6,7]. Amplification of BCL6 is observed in 1% or less of Wilms tumor (2 in 136 cases) and B-lymphoblastic leukemia/lymphoma (1 in 731 cases)[6,7].

Potential relevance: B-cell lymphoma with BCL6 translocations that co-occur with MYC are referred to as double-hit lymphoma (DHL), while co-occurrence with MYC and BCL2 rearrangements is referred to as triple-hit lymphoma[83]. Such concomitant rearrangements are recognized by the World Health Organization (WHO) as diagnostic entity of diffuse large B-cell lymphoma/high grade B-cell lymphoma (HGBL) with MYC and BCL2 rearrangements[84]. DHL expressing BCL6 rearrangements are most often aggressive with poor prognosis, involve extra nodal sites, and have a germinal center phenotype[85,86].

CDKN2A p.(R103Vfs*34) c.306_333delGCGGCTGGACGTGCGCGATGCCTGGGGC

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)[49]. The INK4 family regulates cell cycle progression by inhibiting CDK4 or CDK6, thereby preventing the phosphorylation of Rb[50,51,52]. CDKN2A encodes two alternative transcript variants, namely p16 and p14ARF, both of which exhibit differential tumor suppressor functions[53]. 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[1,53,54]. CDKN2A aberrations commonly co-occur with CDKN2B[49]. Loss of CDKN2A/p16 results in downstream inactivation of the Rb and p53 pathways, leading to uncontrolled cell proliferation[55]. Germline mutations of CDKN2A are known to confer a predisposition to melanoma and pancreatic cancer[56,57].

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[58]. 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[6,7]. 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[6,7]. Alterations in CDKN2A are also observed in pediatric cancers[7]. 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[7]. 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)[7].

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[8,59,60]. Additionally, deletion of CDKN2B is a molecular marker used in staging Grade 4 pediatric IDH-mutant astrocytoma[61]. 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[62,63,64]. Alternatively, CDKN2A expression and Rb inactivation demonstrate resistance to palbociclib in cases of glioblastoma multiforme[65]. 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[66,67,68,69].

KMT2D c.14382+1G>A

lysine methyltransferase 2D

Background: The KMT2D gene encodes the lysine methyltransferase 2D protein, a transcriptional coactivator and histone H3 lysine 4 (H3K4) methyltransferase[1]. KMT2D belongs to the SET domain protein methyltransferase superfamily[70]. KMT2D is known to be involved in the regulation of cell differentiation, metabolism, and tumor suppression due to its methyltransferase activity[70]. Mutations or deletions in the enzymatic SET domain of KMT2D are believed to result in loss of function and may contribute to defective enhancer regulation and altered gene expression[70].

Alterations and prevalence: Somatic mutations in KMT2D are predominantly missense or truncating and are observed in 29% of diffuse large B-cell lymphoma (DLBCL), 28% of bladder urothelial carcinoma, 27% of uterine corpus endometrial carcinoma, 22% of lung squamous cell carcinoma, 21% of skin cutaneous melanoma, 17% of stomach adenocarcinoma, 15% of head and neck squamous cell carcinoma, and 14% of cervical squamous cell carcinoma[6,7].

Biomarker Descriptions (continued)

Potential relevance: Currently, no therapies are approved for KMT2D 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[128]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[129,130]. 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[131]. 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[132]. 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)[132]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[133,134,135,136,137]. 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[130]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[129,130,134,138].

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[129,130,139,140]. 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[139,140].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[141] (2014) and nivolumab[142] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[141] 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[141]. Dostarlimab[143] (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[135,144]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[145] (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[135,146,147]. 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[147]. 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[148,149]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[148,149].

NFE2L2 p.(R34G) c.100C>G

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)[124]. NFE2L2 targets include genes involved in antioxidant response, drug metabolism, DNA repair, autophagy, cell survival, and proliferation[124,125]. NFE2L2 is negatively regulated by KEAP1, a Cul3 adaptor protein, that ubiquitinates NFE2L2[125].

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[6,7]. 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[124,126].

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)[127], 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.

NOTCH2 p.(P6Rfs*27) c.17_18delCC

notch 2

Background: The NOTCH2 gene encodes the notch receptor 2 protein, a type 1 transmembrane protein and member of the NOTCH family of genes, which also includes NOTCH1, NOTCH3, and NOTCH4. NOTCH proteins contain multiple epidermal growth factor (EGF)-like repeats in their extracellular domain, which are responsible for ligand binding and homodimerization, thereby promoting NOTCH signaling[20]. Following ligand binding, the NOTCH intracellular domain is released, which activates the transcription of several

Biomarker Descriptions (continued)

genes involved in regulation of cell proliferation, differentiation, growth, and metabolism[21,22]. In cancer, depending on the tumor type, aberrations in the NOTCH family can be gain of function or loss of function suggesting both oncogenic and tumor suppressor roles for NOTCH family members[23,24,25,26].

Alterations and prevalence: Somatic mutations observed in NOTCH2 are primarily missense or truncating and are found in about 11% of uterine cancer, 6% of melanoma and stomach cancer, as well as 3-5% diffuse large B-cell lymphoma (DLBCL), lung, colorectal, bladder, cervical, and head and neck cancers[6].

Potential relevance: Currently, no therapies are approved for NOTCH2 aberrations.

TP53 p.(Y236*) c.708C>G

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[104]. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential[105]. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers[106,107].

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%)[6,7,108,109,110,111]. 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[6,7]. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes[112,113,114,115]. Alterations in TP53 are also observed in pediatric cancers[6,7]. 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)[6,7]. Biallelic loss of TP53 is observed in 10% of bone cancer, 2% of Wilms tumor, and less than 1% of B-lymphoblastic leukemia/lymphoma (2 in 731 cases) and leukemia (1 in 250 cases)[6,7].

Potential relevance: The small molecule p53 reactivator, PC14586[116] (2020), received a fast track designation by the FDA for advanced tumors harboring a TP53 Y220C mutation. The FDA has granted fast track designation to the p53 reactivator, eprenetapopt[117], (2019) and breakthrough designation[118] (2020) in combination with azacitidine or azacitidine and venetoclax for acute myeloid leukemia patients (AML) and myelodysplastic syndrome (MDS) harboring a TP53 mutation, respectively. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation[119,120]. TP53 mutation are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma[18]. 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)[33,34,35,38,46,121]. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant[122]. 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[123].

YAP1 amplification

Yes associated protein 1

Background: The YAP1 gene encodes the Yes1 associated transcriptional regulator[1]. YAP1 functions as a transcriptional coactivator for TEAD transcription factors and is an important effector of the Hippo signaling pathway[2]. The Hippo pathway is considered a tumor suppressor pathway due to its involvement in various cellular processes including cell proliferation, apoptosis, stem cell expansion, and negative regulation of YAP1[2,3]. Aberrations in YAP1, including upregulation, have been associated with tumorigenesis and shorter survival[3,4]. Germline mutations, specifically R331W, have been associated with an increased risk for lung adenocarcinoma[5].

Alterations and prevalence: Somatic mutations in YAP1 are observed in 3% of uterine corpus endometrial carcinoma, 2% of skin cutaneous melanoma, esophageal adenocarcinoma, kidney chromophobe, and 1% of uveal melanoma, kidney renal papillary cell carcinoma, lung squamous cell carcinoma, cervical squamous cell carcinoma, and colorectal adenocarcinoma[6,7]. Amplification of YAP1 is observed in 10% of cervical squamous cell carcinoma, 5% of head and neck squamous cell carcinoma and ovarian cystadenocarcinoma, and 3% of bladder urothelial carcinoma, sarcoma, and esophageal adenocarcinoma[6,7]. YAP1 fusions are observed in 1% of sarcoma, esophageal adenocarcinoma, cervical squamous cell carcinoma, skin cutaneous melanoma, and head and neck squamous cell carcinoma[6,7].

Biomarker Descriptions (continued)

Potential relevance: Currently, no therapies are approved for YAP1 aberrations. YAP1::TFE3 fusion is considered an ancillary diagnostic marker for epithelioid hemangioendothelioma[8]. Overexpression of YAP1 is a poor prognostic marker in hepatocellular carcinoma, gastric cancer, colorectal cancer, non-small cell lung cancer, and small cell lung cancer[2].

MPL amplification

MPL proto-oncogene, thrombopoietin receptor

Background: The MPL gene encodes the MPL proto-oncogene, a transmembrane thrombopoietin receptor. Binding of the cytokine thrombopoietin to MPL leads to JAK2 activation and subsequent signaling that regulates stem cell homeostasis, cell survival, and proliferation[71]. Mutations in MPL typically disrupt normal auto-inhibitory functions and result in subsequent ligand-independent thrombopoietin receptor activation[71]. Gain-of-function mutations in MPL are associated with myeloproliferative neoplasms (MPN) and hereditary thrombocytosis. Loss-of-function mutations are linked to bone marrow failure syndromes, due to the regulation of thrombopoiesis by thrombopoietin[72].

Alterations and prevalence: Somatic mutations in MPL are present in 3-5% of primary myelofibrosis (PMF)[71,73]. Specifically, MPL W515L/K mutations are reported in 5-8% of myelofibrosis (MF) and 1-4% of essential thrombocythemia (ET)[34]. Other observed MPL mutations include V501A, Y252H, and S204P[71].

Potential relevance: MPL W515K/L mutations confer intermediate prognosis in MPN[34].

MECOM amplification

MDS1 and EVI1 complex locus

Background: The MECOM gene encodes the MDS1 and EVI1 complex locus (MECOM), a zinc-finger transcriptional factor that regulates hematopoietic cell differentiation[27]. The MECOM locus encodes multiple alternative splice variants that result in MDS1-EVI1, MDS1, and EVI1 protein isoforms[28]. The EVI1 isoform is the most abundant and oncogenic form of MECOM that is expressed in various cancers including acute myeloid leukemia (AML)[28,29]. MECOM is a frequent target of chromosomal translocation which can lead to MECOM overexpression and leukemogenesis[30].

Alterations and prevalence: Somatic mutations MECOM are observed in up to 22% of malignant melanoma; 75% of these mutations are missense and the remaining 25% are truncating mutations[6,7,31]. MECOM amplifications are observed in up to 35% of lung squamous cell carcinoma, 30% of ovarian serous cystadenocarcinoma, and 20% of esophageal adenocarcinoma, uterine carcinosarcoma, and cervical squamous cell carcinoma[6,7]. MECOM rearrangements occur with various partner genes including ETV6, RUNX1, and H2AFY[32]. The t(3;21)(q26;q22) translocation that results in the MECOM::RUNX1 fusion is most commonly observed in chronic myeloid leukemia (CML) in blast crisis. The t(3;3)(q21.3;q26.2)/ inv(3)(q21.3;q26.3) translocation, also referred to as inv(3)/t(3;3), results in a GATA2::MECOM fusion and is observed in AML, primary myelofibrosis (PMF), and myelodysplastic syndrome (MDS)[33,34,35]. The inv(3)/ t(3;3) translocation repositions the distal GATA enhancer element and activates MECOM expression while simultaneously causing GATA2 haploinsufficiency[36].

Potential relevance: AML with MECOM rearrangement is considered a distinct molecular subtype of AML as defined by the World Health Organization (WHO)[37]. MECOM rearrangements, including GATA2::MECOM fusions, are associated with poor/adverse risk in AML[33,38]. Inv(3) is associated with poor cytogenetic risk in MDS as defined by the revised international prognostic scoring system (IPSS-R) scoring system[35]. In PMF, inv(3) is considered an unfavorable karyotype associated with intermediate risk as defined by the dynamic international prognostic scoring system (DIPSS)-Plus scoring system[34]. MECOM overexpression is observed in 10% of de novo AML associated with poor prognosis, and is commonly found in MLL-rearranged cases[39,40]. Amplification of MECOM is associated with favorable prognosis in ovarian cancer[41].

IL7R amplification

interleukin 7 receptor

Background: The IL7R gene encodes the interleukin 7 receptor[1]. IL7R is commonly expressed in immune cells and plays a critical role in the development and homeostasis of the immune system, including the regulation of cell development, survival, and differentiation of T-cells[42,43]. IL7R may also play a role in the development of B-cells by controlling downstream signaling pathways, including the JAK/ PI3K/AKT pathways[43]. Mutations and other aberrations in IL7R result in a gain-of-function, thereby supporting its oncogenic role[44].

Alterations and prevalence: Somatic mutations in IL7R are observed in 13% of skin cutaneous melanoma, 6% of lung squamous cell carcinoma, and 4% of uterine corpus endometrial carcinoma, lung adenocarcinoma, and stomach adenocarcinoma[6,7]. Amplification of IL7R is observed in 10% of lung squamous cell carcinoma, 9% of lung adenocarcinoma, 8% of esophageal adenocarcinoma, 7% of bladder urothelial carcinoma, 6% of stomach adenocarcinoma, and 5% of cervical squamous cell carcinoma and ovarian serous cystadenocarcinoma[6,7]. Alterations in IL7R are also observed in pediatric cancers[6,7]. Somatic mutations are observed in 5% of T-

Biomarker Descriptions (continued)

lymphoblastic leukemia/lymphoma, 3% of soft tissue sarcoma (1 in 38 cases), 2% of B- lymphoblastic leukemia/lymphoma (4 in 252 cases), and less than 1% of embryonal tumor (3 in 332 cases), glioma (2 in 297 cases), leukemia (2 in 311 cases), bone cancer (2 in 327 cases), and peripheral nervous system cancers (1 in 1158 cases)[6,7,45]. Amplification of IL7R is observed in about 5% of pediatric bone cancer[6,7].

Potential relevance: Currently, no therapies are approved for IL7R aberrations. The Philadelphia-chromosome-like (Ph-like) phenotype of acute lymphoblastic leukemia (ALL) is associated with mutations in tyrosine kinase pathway genes, including IL7R[45,46,47]. Testing for these abnormalities at diagnosis may aid in risk stratification[46]. Notably, mutations in IL7R are associated with unfavorable-risk features in pediatric acute lymphoblastic leukemia[47,48].

AR amplification

androgen receptor

Background: The AR gene encodes the androgen receptor protein (AR), a ligand-activated transcription factor regulated by the binding of the hormones testosterone and dihydrotestosterone[90,91]. Hormone binding to AR results in receptor dimerization, nuclear translocation, and target gene transcription, thus activating the RAS/RAF/MEK/ERK and PI3K/AKT/MTOR signaling pathways, which promote cell proliferation and survival[91,92,93].

Alterations and prevalence: Alterations in AR function can result from overexpression, gene amplification, or mutations. AR mutations, including L702H, W742C/L, H875Y, and T878A, are commonly observed in 10-30% of castration-resistant prostate cancer and result in decreased ligand specificity, allowing other nuclear hormones to activate AR[94]. Androgen receptor splice variants have been reported in castration resistant prostate cancer[95,96]. The androgen receptor splice variant 7 (AR-V7) is a result of aberrant mRNA splicing of AR exons 1-3 and a cryptic exon 3, resulting in the expression of a constitutively active protein[96].

Potential relevance: The FDA has granted fast track designation (2022) to the selective androgen receptor targeting agonist, enobosarm, for the treatment of patients with androgen AR-positive, estrogen receptor (ER)-positive, HER2-negative metastatic breast cancer[97]. The FDA also granted fast track designation (2016) to the small-molecule CYP17 lyase-selective inhibitor, seviteronel, for AR-positive triple-negative breast cancer (TNBC) patients[98]. Androgen deprivation therapy (ADT) such as abiraterone[99] (2011) and enzalutamide[100] (2011) are FDA approved for use in locally advanced and metastatic prostate cancers. Other ADT therapies including leuprolide and bicalutamide are specifically recommended in AR+ unresectable metastatic salivary gland tumors[101]. Although many men initially respond to ADT, most will develop hormone resistance. Resistance to ADT is also associated with other aberrations of the AR gene including mutations within the ligand binding domain and gene amplification[94,102,103]. The androgen receptor splice variant, AR-V7, lacks the ligand binding domain, resulting in constitutive activation and is associated with resistance to androgen deprivation therapy (ADT) in advanced prostate cancer[95].

ZMYM3 deletion

zinc finger MYM-type containing 3

Background: The ZMYM3 gene encodes the zinc finger MYM-type containing 3 protein[1]. While the function is not fully understood, ZMYM3 is capable of binding histones and DNA, and may facilitate the repair of double-strand breaks (DSBs)[74].

Alterations and prevalence: Somatic mutations in ZMYM3 are observed in 12% of uterine corpus endometrial carcinoma, 5% of skin cutaneous melanoma, 4% of colorectal adenocarcinoma, 3% of lung adenocarcinoma, lung squamous cell carcinoma, cervical squamous cell carcinoma, esophageal adenocarcinoma, and bladder urothelial carcinoma[6,7]. In prostate cancer, ZMYM3 mutations have been observed to be enriched in African American men compared to white men with one study demonstrating occurrence in 11.7% vs. 2.7% of patients, respectively[75]. Biallelic deletion of ZMYM3 is observed in 3% of cholangiocarcinoma and 2% of sarcoma and kidney chromophobe[6,7].

Potential relevance: Currently, no therapies are approved for ZMYM3 aberrations.

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,

Genes Assayed (continued)

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

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

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

ATRX deletion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
pamiparib, tislelizumab	✖	✖	✖	✖	● (II)

MYCL amplification

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
MRT-2359	✖	✖	✖	✖	● (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	***52.15%***
BRCA2	***LOH, 13q13.1(32890491-32972932)x2***
BARD1	***LOH, 2q35(215593375-215674382)x2***

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

Thermo Fisher Scientific's Ion Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.1.1 data version 2025.06(006)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-05-14. NCCN information was sourced from www.nccn.org and is current as of 2025-05-01. EMA information was sourced from www.ema.europa.eu and is current as of 2025-05-14. ESMO information was sourced from www.esmo.org and is current as of 2025-05-01. Clinical Trials information is current as of 2025-05-01. 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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