

Patient Name: 김동영
Gender: M
Sample ID: N26-59

Primary Tumor Site: lung
Collection Date: 2026.01.26

Sample Cancer Type: Lung Cancer

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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	6.66 Mut/Mb measured

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	CDKN2A deletion cyclin dependent kinase inhibitor 2A Locus: chr9:21968178	None*	None*	5
IIC	CDKN2B deletion cyclin dependent kinase inhibitor 2B Locus: chr9:22005728	None*	None*	2
IIC	ARID1A p.(Q802Sfs*15) c.2402_2403insG AT-rich interaction domain 1A Allele Frequency: 30.95% Locus: chr1:27088787 Transcript: NM_006015.6	None*	None*	1

* Public data sources included in relevant therapies: FDA1, NCCN, EMA2, 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

Microsatellite stable, PTPN11 p.(G503W) c.1507G>T, TP53 p.(E294*) c.880G>T, TGFBR2 p.(W529*) c.1586G>A, CARD11 amplification, RAC1 amplification, NQO1 p.(P187S) c.559C>T, Tumor Mutational Burden

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
ARID1A	p.(Q802Sfs*15)	c.2402_2403insG	.	chr1:27088787	30.95%	NM_006015.6	frameshift Insertion
PTPN11	p.(G503W)	c.1507G>T	COSM5945283	chr12:112926887	25.24%	NM_002834.5	missense
TP53	p.(E294*)	c.880G>T	.	chr17:7577058	26.87%	NM_000546.6	nonsense
TGFBR2	p.(W529*)	c.1586G>A	.	chr3:30729990	26.82%	NM_001024847.2	nonsense
NQO1	p.(P187S)	c.559C>T	.	chr16:69745145	36.87%	NM_000903.3	missense
JAK1	p.(L910Q)	c.2729T>A	.	chr1:65305399	19.51%	NM_002227.4	missense
KIT	p.(V921F)	c.2761G>T	.	chr4:55603405	10.30%	NM_000222.3	missense
CARD11	p.(?)	c.3019+3G>A	.	chr7:2952918	4.16%	NM_032415.7	unknown
MGAM2	p.(G1479V)	c.4436G>T	.	chr7:141896043	23.27%	NM_001293626.2	missense
RUNX1	p.(R471H)	c.1412G>A	.	chr21:36164463	26.95%	NM_001754.5	missense

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
CDKN2A	chr9:21968178	0	0.6
CDKN2B	chr9:22005728	0	0.59
CARD11	chr7:2949684	5.63	1.73
RAC1	chr7:6426823	5.45	1.69
SETBP1	chr18:42281265	0	0.59

Biomarker Descriptions

CDKN2A deletion

cyclin dependent kinase inhibitor 2A

Background: CDKN2A encodes cyclin dependent kinase inhibitor 2A, a cell cycle regulator that controls G1/S progression¹. 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)⁸³. The INK4 family regulates cell cycle progression by inhibiting CDK4 or CDK6, thereby preventing the phosphorylation of Rb^{84,85,86}. CDKN2A encodes two alternative transcript variants, namely p16 and p14ARF, both of which exhibit differential tumor suppressor functions⁸⁷. 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^{1,87,88}. CDKN2A aberrations commonly co-occur with CDKN2B⁸³. Loss of CDKN2A/p16 results in downstream inactivation of the Rb and p53 pathways, leading to uncontrolled cell proliferation⁸⁹. Germline mutations of CDKN2A are known to confer a predisposition to melanoma and pancreatic cancer^{90,91}.

Biomarker Descriptions (continued)

Alterations and prevalence: Somatic alterations in CDKN2A often result in loss of function (LOF) which is attributed to copy number loss, truncating, or missense mutations⁹². 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^{13,14}. 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^{13,14}. Alterations in CDKN2A are also observed in pediatric cancers¹⁴. 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 tumors¹⁴. Somatic mutations in CDKN2A are observed in less than 1.5% of bone cancer (5 in 327 cases), B-lymphoblastic leukemia/lymphoma (3 in 252 cases), and leukemia (1 in 354 cases)¹⁴.

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^{93,94,95}. Additionally, deletion of CDKN2B is a molecular marker used in staging Grade 4 pediatric IDH-mutant astrocytoma⁹⁶. 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^{97,98,99}. Alternatively, CDKN2A expression and Rb inactivation demonstrate resistance to palbociclib in cases of glioblastoma multiforme¹⁰⁰. 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^{101,102,103,104}.

CDKN2B deletion

cyclin dependent kinase inhibitor 2B

Background: CDKN2B encodes cyclin dependent kinase inhibitor 2B, a cell cycle regulator that controls G1/S progression^{1,83}. CDKN2B, also known as p15/INK4B, belongs to a family of INK4 cyclin-dependent kinase inhibitors, which also includes CDKN2A (p16/INK4A), CDKN2C (p18/INK4C), and CDKN2D (p19/INK4D)⁸³. The INK4 family regulates cell cycle progression by inhibiting CDK4 or CDK6, thereby preventing the phosphorylation of Rb^{84,85,86}. CDKN2B is a tumor suppressor and aberrations in this gene commonly co-occur with CDKN2A⁸³. Germline mutations in CDKN2B are linked to pancreatic cancer predisposition and familial renal cell carcinoma^{1,105,106}.

Alterations and prevalence: CDKN2B copy number loss is a frequently occurring somatic aberration that is observed in 55% of glioblastoma multiforme, 43% of mesothelioma, 35% of esophageal adenocarcinoma, 31% of bladder urothelial carcinoma, 29% of skin cutaneous melanoma, 28% of head and neck squamous cell carcinoma, 27% of pancreatic adenocarcinoma, 26% of lung squamous cell carcinoma, 25% of diffuse large B-cell lymphoma, 16% of lung adenocarcinoma, 15% of sarcoma, 14% of cholangiocarcinoma, 11% of stomach adenocarcinoma and brain lower grade glioma, 5% of liver hepatocellular carcinoma, 4% of adrenocortical carcinoma, breast invasive carcinoma, thymoma, and kidney renal papillary cell carcinoma, 3% of kidney renal clear cell carcinoma and ovarian serous cystadenocarcinoma, and 2% of uterine carcinosarcoma and kidney chromophobe^{13,14}. Somatic mutations in CDKN2B are observed in 2% of uterine carcinosarcoma^{13,14}. CDKN2B copy number loss is also observed in pediatric cancers, including 64% of childhood T-lymphoblastic leukemia/lymphoma, 37% of pediatric B-lymphoblastic leukemia/lymphoma, 25% of pediatric gliomas, 14% of pediatric bone cancers, 6% of embryonal tumors, and 2% of peripheral nervous system cancers^{13,14}. Somatic mutations in CDKN2B are observed in less than 1% of bone cancer (1 in 327 cases)^{13,14}.

Potential relevance: Currently, no therapies are approved for CDKN2B aberrations. Homozygous deletion of CDKN2B is a molecular marker used in staging grade 4 pediatric IDH-mutant astrocytoma⁹⁶.

ARID1A p.(Q802Sfs*15) c.2402_2403insG

AT-rich interaction domain 1A

Background: The ARID1A gene encodes the AT-rich interaction domain 1A tumor suppressor protein¹. ARID1A, also known as BAF250A, belongs to the ARID1 subfamily that also includes ARID1B^{1,77}. ARID1A and ARID1B are mutually exclusive subunits of the BAF variant of the SWI/SNF chromatin-remodeling complex^{77,78}. The BAF complex is a multisubunit protein that consists of SMARCB1/IN1, SMARCC1/BAF155, SMARCC2/BAF170, SMARCA4/BRG1 or SMARCA2/BRM, and ARID1A or ARID1B⁷⁸. The BAF complex remodels chromatin at promoter and enhancer elements to alter and regulate gene expression^{78,79}. ARID1A binds to transcription factors and coactivator/corepressor complexes to alter transcription⁷⁷. Recurrent inactivating mutations in BAF complex subunits, including ARID1A, lead to transcriptional dysfunction thereby, altering its tumor suppressor function⁷⁷.

Biomarker Descriptions (continued)

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 tumors⁷⁹. The majority of ARID1A inactivating mutations are nonsense or frameshift mutations⁷⁷. 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^{13,14,78}. 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 response⁸⁰. Biallelic deletion of ARID1A is observed in 3% of cholangiocarcinoma and stomach adenocarcinoma, and 2% of pheochromocytoma and paraganglioma^{13,14}. Alterations in ARID1A are also observed in pediatric cancers¹⁴. 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)¹⁴. 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)¹⁴.

Potential relevance: Currently, no therapies are approved for ARID1A aberrations. However, the FDA has granted fast track designation (2022) to HSF1 pathway inhibitor, NXP-800⁸¹, for the treatment of platinum resistant ARID1A-mutated ovarian carcinoma. Tulumimostat⁸², 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.

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 genome⁴⁴. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue^{45,46}. MSI is closely tied to the status of the mismatch repair (MMR) genes. In humans, the core MMR genes include MLH1, MSH2, MSH6, and PMS2⁴⁷. 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 D17S250⁴⁸. 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)⁴⁸. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS^{49,50,51,52,53}. 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 genes⁴⁶. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer^{45,46,50,54}.

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^{45,46,55,56}. 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^{55,56}.

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab⁵⁷ (2014) and nivolumab⁵⁸ (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab⁵⁷ 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 indication⁵⁷. Dostarlimab⁵⁹ (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^{51,60}. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab⁶¹ (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^{51,62,63}. 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 patients⁶³. 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^{64,65}. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers^{64,65}.

PTPN11 p.(G503W) c.1507G>T

protein tyrosine phosphatase, non-receptor type 11

Background: The PTPN11 gene encodes a tyrosine phosphatase non-receptor type 11 protein, and is also known as Src homology region 2 domain-containing phosphatase-2 (SHP-2)^{1,2}. PTPN11 is a member of the protein tyrosine phosphatase (PTP) family that is ubiquitously expressed and regulates cellular growth, differentiation, mitotic cycle, and oncogenic transformation³. PTPN11 contains

Biomarker Descriptions (continued)

two tandem N-terminal Src homology-2 domains (N-SH2 and C-SH2), a PTP catalytic domain, and uncharacterized C-terminal domain⁴. PTPN11 regulates various signaling processes including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, and JAK/STAT pathways^{5,6}. Germline mutations in PTPN11 are associated with LEOPARD syndrome and Noonan syndrome with a predisposition to juvenile myelomonocytic leukemia (JMML) or myeloproliferative neoplasms (MPN)^{7,8}. Somatic mutations in PTPN11 are associated with JMML^{9,10} and solid tumors such as lung, colon, and thyroid^{4,11}.

Alterations and prevalence: Somatic alterations in PTPN11 include mutations and amplification^{7,12}. Somatic mutations in PTPN11 occur in 5% uterine corpus endometrial carcinoma and acute myeloid leukemia, 3% of skin cutaneous melanoma, glioblastoma multiforme, and colorectal adenocarcinoma, and 2% of stomach adenocarcinoma, uterine carcinosarcoma, lung adenocarcinoma, and brain lower grade glioma^{13,14}. Mutations including E76K and D61Y result in PTPN11 activation and are associated with 30% of JMML⁶. PTPN11 fusion is observed in 2% of uterine carcinosarcoma^{13,14}. Amplification of PTPN11 is observed in 2% of bladder urothelial carcinoma, sarcoma, uterine carcinosarcoma, and esophageal adenocarcinoma^{13,14}. Alterations in PTPN11 are also observed in pediatric cancers¹⁴. Somatic mutations in PTPN11 are observed in 4% of leukemia (15 in 354 cases), 3% of B-lymphoblastic leukemia/lymphoma (7 in 252 cases) and soft tissue sarcoma (1 in 38 cases), 2% of T-lymphoblastic leukemia/lymphoma (1 in 41 cases), 1% of glioma (3 in 297 cases), and less than 1% of peripheral nervous system tumors (7 in 1158 cases) and bone cancer (1 in 327 cases)¹⁴.

Potential relevance: Currently, no therapies are approved for PTPN11 aberrations. Somatic mutations in PTPN11 confer drug resistance to venetoclax and azacitidine in AML^{15,16}.

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

tumor protein p53

Background: The TP53 gene encodes the tumor suppressor protein p53, which binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair¹. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis¹⁷. Alterations in TP53 are required for oncogenesis as they result in loss of protein function and gain of transforming potential¹⁸. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers^{19,20}.

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%)^{13,14,21,22,23,24}. 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^{13,14}. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes^{25,26,27,28}. Alterations in TP53 are also observed in pediatric cancers^{13,14}. 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)^{13,14}. 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)^{13,14}.

Potential relevance: The small molecule p53 reactivator, PC14586²⁹ (2020), received a fast track designation by the FDA for advanced tumors harboring a TP53 Y220C mutation. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation^{30,31}. TP53 mutations are a diagnostic marker of SHH-activated, TP53-mutant medulloblastoma³². 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)^{8,33,34,35,36}. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant³⁷. 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 system³⁸.

TGFBR2 p.(W529*) c.1586G>A

transforming growth factor beta receptor 2

Background: TGFBR2 encodes transforming growth factor beta receptor 2¹. Along with TGFBR1 and TGFBR3, TGFBR2 is a member of the TGF-beta receptor family³⁹. Both TGFBR1 and TGFBR2 function as serine/threonine and tyrosine kinases, whereas TGFBR3 does not possess any kinase activity³⁹. TGFBR1 heterodimerizes with TGFBR2 and activates ligand binding of TGF-beta cytokines namely TGFβ1, TGFβ2, and TGFβ3³⁹. Heterodimerization with TGFBR2 enables TGFBR1 to phosphorylate downstream SMAD2/3, which leads to activation of SMAD4⁴⁰. This process regulates various signaling pathways implicated in cancer initiation and progression, including epithelial to mesenchymal transition (EMT) and apoptosis^{41,42,43}.

Biomarker Descriptions (continued)

Alterations and prevalence: Somatic mutations in TGFBR2 are observed in 5% of esophageal adenocarcinoma, and head and neck squamous cell carcinoma, 4% of pancreatic adenocarcinoma, stomach adenocarcinoma, uterine corpus endometrial carcinoma, colorectal adenocarcinoma, and cholangiocarcinoma^{13,14}. Biallelic deletion of TGFBR2 is observed in 3% of kidney renal clear cell carcinoma and 2% of stomach adenocarcinoma and head and neck squamous cell carcinoma^{13,14}.

Potential relevance: Currently, no therapies are approved for TGFBR2 aberrations.

CARD11 amplification

caspase recruitment domain family member 11

Background: The CARD11 gene encodes caspase recruitment domain family member 11 protein¹. CARD11, also known as CARMA1, is a scaffold protein that functions in the adaptive immune system to mediate antigen-receptor signaling through the NF- κ B, JNK, and MTOR signaling pathways^{74,75,76}. In response to T- or B- cell receptor triggering, CARD11 is activated, which results in binding of various cofactors, including BCL10, MALT1, and RNF31⁷⁵. Cofactor recruitment to CARD11 leads to the ubiquitination of BCL10, which then associates with the I κ B (IKK) complex through the IKK γ subunit, thereby leading to I κ B activation and downstream NF- κ B signaling⁷⁵. CARD11 gain-of-function mutations are associated with constitutive activation of NF- κ B signaling and aberrant proliferation of diffuse large B-cell lymphoma (DLBCL), supporting an oncogenic role for CARD11⁷⁵.

Alterations and prevalence: Somatic mutations in CARD11 are observed in 17% of DLBCL, 14% of skin cutaneous melanoma, 10% of uterine corpus endometrial carcinoma, 7% of colorectal adenocarcinoma and stomach adenocarcinoma, and 6% of lung adenocarcinoma^{13,14}. Amplification of CARD11 is observed in 5% of esophageal adenocarcinoma, 4% of bladder urothelial carcinoma, lung adenocarcinoma, and uterine carcinosarcoma, 3% of stomach adenocarcinoma, 2% of adrenocortical carcinoma, DLBCL, and skin cutaneous melanoma^{13,14}.

Potential relevance: Currently, no therapies are approved for CARD11 aberrations.

RAC1 amplification

ras-related C3 botulinum toxin substrate 1 (rho family, small GTP binding protein Rac1)

Background: The RAC1 gene encodes Rac family small GTPase 1¹. RAC1 is one of 23 members of the RHO subfamily of GTPases within the RAS superfamily^{66,67,68}. The RAS superfamily includes the RHO, RAS, RAB, ARF, RHEB, and Ga subfamilies^{66,67,68,69}. RHO subfamily members are known for the regulation of several pathways involved in cell morphology, motility, and proliferation^{70,71,72}. RAC1 can exist in an inactive GDP-bound form as well as in an active GTP-bound form⁶⁸. Guanine nucleotide exchange factors (GEFs) activate RAC1 by facilitating the release of GDP to allow for binding of GTP, while GTPase-activating proteins (GAPs) facilitate the reverse, that is converting GTP-bound RAC1 to an inactive state⁶⁸.

Alterations and prevalence: Somatic mutations in RAC1 are observed in 6% of skin cutaneous melanoma and 2% of uterine carcinosarcoma^{13,14}. The P29S mutation is recurrent in melanoma and is potentially associated with resistance to BRAF inhibitors^{13,14,73}. RAC1 is amplified in 6% of esophageal squamous cell carcinoma, 4% of uterine carcinosarcoma, bladder urothelial carcinoma, and sarcoma, as well as 2% of skin cutaneous melanoma and esophageal adenocarcinoma^{13,14}.

Potential relevance: Currently, no therapies are approved for RAC1 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, CTNNA1, 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, MYO10, 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, PXDN, RAC1, RAF1, RARA, RET, RGS7, RHEB, RHOA, RICTOR, RIT1, ROS1, RPL10, SETBP1, SF3B1, SIX1, SIX2, SLC01B3, SMC1A, SMO,

Genes Assayed (continued)

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

SNCAIP, SOS1, SOX2, SPOP, SRC, SRSF2, STAT3, STAT5B, STAT6, TAF1, TERT, TGFB1, 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, CBF, 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, ERRF1, 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, PLAG1, PMS1, PMS2, POLD1, POLE, POT1, PPM1D, PPP2R1A, PPP2R2A, PPP6C, PRDM1, PRDM9, PRKACA, PRKAR1A, PTCH1, PTEN, PTPN11, PTPRT, PXDN, 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, SLC1B3, SLX4, SMAD2, SMAD4, SMARCA4, SMARCB1, SMC1A, SMO, SOX9, SPEN, SPOP, SRC, STAG2, STAT3, STAT6, STK11, SUFU, TAP1, TAP2, TBX3, TCF7L2, TERT, TET2, TGFB2, TNFAIP3, TNFRSF14, TOP1, TP53, TP63, TPMT, TPP2, TSC1, TSC2, U2AF1, USP8, USP9X, VHL, WT1, XPO1, XRCC2, XRCC3, YAP1, YES1, ZFH3, 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, CBF, 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, ERRF1, 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, TGFB2, TMEM132D, TNFAIP3, TNFRSF14, TP53, TP63, TPP2, TSC1, TSC2, UGT1A1, USP9X, VHL, WT1, XRCC2, XRCC3, ZBTB20, ZFH3, ZMYM3, ZRSR2

Relevant Therapy Summary

In this cancer type
 In other cancer type
 In this cancer type and other cancer types
 No evidence

CDKN2A deletion

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

CDKN2B deletion

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

ARID1A p.(Q802Sfs*15) c.2402_2403insG

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

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

HRR Details

Gene/Genomic Alteration	Finding
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 OncoPrint Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on OncoPrint Reporter (6.2.4 data version 2025.12(007)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-11-25. NCCN information was sourced from www.nccn.org and is current as of 2025-11-03. EMA information was sourced from www.ema.europa.eu and is current as of 2025-11-25. ESMO information was sourced from www.esmo.org and is current as of 2025-11-03. Clinical Trials information is current as of 2025-11-03. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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