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Patient Name: 이순자
Gender: F
Sample ID: N25-240

Primary Tumor Site: Lung
Collection Date: 2025.09.10.

Sample Cancer Type: Lung Cancer

Report Highlights

2 Relevant Biomarkers
4 Therapies Available
36 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	***TPM3::ROS1 fusion***
MET	None detected		

Genomic Alteration	Finding
Tumor Mutational Burden	***9.48 Mut/Mb measured***

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*TPM3::ROS1 fusion* tropomyosin 3 - ROS proto-oncogene 1, receptor tyrosine kinase Locus: chr1:154142876 - chr6:117642557	**crizotinib** [1, 2 / I, II+] **entrectinib** [1, 2 / I, II+] **repotrectinib** [1, 2 / I, II+] lorlatinib [II+]	crizotinib [II+] entrectinib [II+]	35
IIC	*ARID1A p.(Q548*) c.1642C>T* AT-rich interaction domain 1A Allele Frequency: 22.70% Locus: chr1:27057934 Transcript: NM_006015.6	None*	None*	1

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

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

TPM3::ROS1 fusion	**taletrectinib** [1], **zidesamtinib** [1]

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

Prevalent cancer biomarkers without relevant evidence based on included data sources
CDKN2A p.(Y129) c.387C>G, Microsatellite stable, HLA-B deletion, Tumor Mutational Burden*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
ARID1A	p.(Q548*)	c.1642C>T	.	chr1:27057934	22.70%	NM_006015.6	nonsense
CDKN2A	p.(Y129*)	c.387C>G	.	chr9:21970971	28.31%	NM_001195132.2	nonsense
RGS7	p.(E387Q)	c.1159G>C	.	chr1:240969550	11.35%	NM_002924.6	missense
CLOCK	p.(S582F)	c.1745C>T	.	chr4:56310011	22.22%	NM_004898.4	missense
RAD50	p.(E526Q)	c.1576G>C	.	chr5:131927039	9.45%	NM_005732.4	missense
MLIP	p.(V159*)	c.474_475delTGinsCTGA	.	chr6:53989525	5.21%	NM_138569.2	nonsense
ARID1B	p.(R981Q)	c.2942G>A	.	chr6:157469899	11.30%	NM_001371656.1	missense
TSC1	p.(S1043dup)	c.3109_3110insGCA	.	chr9:135772007	40.02%	NM_000368.5	nonframeshift Insertion
SMARCA4	p.(R1135W)	c.3403C>T	.	chr19:11141426	19.05%	NM_001128849.3	missense
ASXL1	p.(D879N)	c.2635G>A	.	chr20:31023150	20.51%	NM_015338.6	missense
ASXL1	p.(E1132K)	c.3394G>A	.	chr20:31023909	21.30%	NM_015338.6	missense

Gene Fusions

Genes	Variant ID	Locus
TPM3::ROS1	TPM3-ROS1.T7R35.COSF1273.1	chr1:154142876 - chr6:117642557

Copy Number Variations

Gene	Locus	Copy Number	CNV Ratio
HLA-B	chr6:31322252	0.27	0.64
PXDNL	chr8:52233342	0.37	0.67
FAM135B	chr8:139144776	0.44	0.68

Biomarker Descriptions

TPM3::ROS1 fusion

ROS proto-oncogene 1, receptor tyrosine kinase, tropomyosin 3

Background: The ROS1 gene encodes the ROS proto-oncogene receptor tyrosine kinase 1, which exhibits structural similarity to anaplastic lymphoma kinase (ALK)[10,11]. Like ALK, ROS1 is the target of recurrent chromosomal rearrangements that generate fusion proteins containing the intact ROS1 tyrosine kinase domain combined with numerous fusion partner genes[12]. ROS1 fusion kinases are constitutively activated and drive oncogenic transformation[13].

Alterations and prevalence: Somatic mutations in ROS1 are observed in 24% of skin cutaneous melanoma, 13% of uterine corpus endometrial carcinoma, 8% of lung squamous cell carcinoma, 7% of colorectal adenocarcinoma, 6% of stomach adenocarcinoma,

Biomarker Descriptions (continued)

5% of bladder urothelial carcinoma, head and neck squamous cell carcinoma, and diffuse large B-cell lymphoma, 4% of lung adenocarcinoma and uterine carcinosarcoma, 3% of adrenocortical carcinoma, esophageal adenocarcinoma, cholangiocarcinoma, cervical squamous cell carcinoma, kidney renal clear cell carcinoma, and glioblastoma multiforme, and 2% of mesothelioma, brain lower grade glioma, breast invasive carcinoma, and acute myeloid leukemia[8,9]. ROS1 fusions are observed in cholangiocarcinoma, gastric cancer, and ovarian cancer and have been reported in approximately 1-2% of non-small cell lung cancer (NSCLC) and glioblastoma[10,14,15,16,17,18]. ROS1 amplification is observed in 3% of sarcoma[8,9]. Alterations in ROS1 are rare in pediatric cancers[8,9]. Somatic mutations are observed in 2% of bone cancer and embryonal tumors, and 1% or less in B-lymphoblastic leukemia/lymphoma (3 in 252 cases), glioma (3 in 297 cases), leukemia (1 in 311 cases), peripheral nervous system tumors (3 in 1158 cases), and Wilms tumor (1 in 710 cases)[8,9]. Amplification of ROS1 is observed in less than 1% of B-lymphoblastic leukemia/lymphoma (1 in 731 cases)[8,9].

Potential relevance: The tyrosine kinase inhibitor (TKI), entrectinib[19] (2019), is approved for the treatment of ROS1 fusion-positive metastatic NSCLC. Crizotinib[20] (2011), originally approved for the treatment of ALK-positive NSCLC, is also approved (2016) for the treatment of ROS1-positive NSCLC[21]. Acquired resistance to crizotinib in ROS1-positive NSCLC is associated with kinase domain mutations S1986F/Y, G2032R, D2033N, and L2155S[22,23,24]. Repotrectinib[25] (2023) is a kinase inhibitor approved for the treatment of locally advanced or metastatic ROS1-positive NSCLC. In 2024, zidesamtinib[26] received breakthrough designation for the treatment of patients with ROS1-positive NSCLC who have been previously treated with two or more ROS1 TKIs. The ROS1 inhibitor, taletrectinib[27] (2022), was also granted breakthrough designation for the treatment of adult patients with advanced or metastatic ROS1-positive NSCLC who are ROS1 tyrosine kinase inhibitor (TKI) treatment-naïve or previously treated with crizotinib. Ceritinib[28] (2017) is a second-generation ALK inhibitor approved for ALK-positive NSCLC that has also shown efficacy in ROS1-positive NSCLC[29]. In a phase II study, ceritinib demonstrated systemic and intra-cranial activity with an objective response rate (ORR) of 62% in patients with advanced ROS1-positive NSCLC[29]. Lorlatinib[30], a CNS-penetrant third-generation ALK and ROS1 inhibitor, is FDA approved (2018) for ALK-positive metastatic NSCLC. Emerging pre-clinical evidence suggests that lorlatinib may target almost all known ALK and ROS1 resistance mutations[31,32]. In a phase I/II study of lorlatinib in advanced ROS1-positive NSCLC, objective responses were observed in both TKI-naïve and those previously treated with crizotinib, regardless of CNS metastasis[33]. Lorlatinib is recommended for subsequent therapy in ROS1 fusion-positive NSCLC patients who have progressed after treatment with crizotinib, entrectinib, or ceritinib[34].

ARID1A p.(Q548*) c.1642C>T

AT-rich interaction domain 1A

Background: The ARID1A gene encodes the AT-rich interaction domain 1A tumor suppressor protein[1]. ARID1A, also known as BAF250A, belongs to the ARID1 subfamily that also includes AR1D1B[1,57]. ARID1A and ARID1B are mutually exclusive subunits of the BAF variant of the SWI/SNF chromatin-remodeling complex[57,58]. 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[58]. The BAF complex remodels chromatin at promoter and enhancer elements to alter and regulate gene expression[58,59]. ARID1A binds to transcription factors and coactivator/corepressor complexes to alter transcription[57]. Recurrent inactivating mutations in BAF complex subunits, including ARID1A, lead to transcriptional dysfunction thereby, altering its tumor suppressor function[57].

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[59]. The majority of ARID1A inactivating mutations are nonsense or frameshift mutations[57]. Somatic mutations in ARID1A have been identified in 50% of ovarian clear cell carcinoma, 30% of endometrioid carcinoma, and 24-43% of uterine corpus endometrial carcinoma, bladder urothelial carcinoma, and stomach adenocarcinoma[8,9,58]. 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[60].

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[61], for the treatment of platinum resistant ARID1A-mutated ovarian carcinoma. Tulmimetostat[62], 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.

CDKN2A p.(Y129*) c.387C>G

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)[63]. The INK4 family regulates cell cycle progression by inhibiting CDK4 or CDK6, thereby preventing the phosphorylation of Rb[64,65,66]. CDKN2A encodes two alternative transcript variants, namely p16 and p14ARF, both of which exhibit differential tumor suppressor functions[67]. 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[1,67,68]. CDKN2A aberrations commonly co-occur with CDKN2B[63]. Loss of CDKN2A/p16 results in downstream inactivation of the Rb and p53 pathways,

Biomarker Descriptions (continued)

leading to uncontrolled cell proliferation[69]. Germline mutations of CDKN2A are known to confer a predisposition to melanoma and pancreatic cancer[70,71].

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[72]. 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[8,9]. 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[8,9]. Alterations in CDKN2A are also observed in pediatric cancers[9]. 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[9]. 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)[9].

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[73,74,75]. Additionally, deletion of CDKN2B is a molecular marker used in staging Grade 4 pediatric IDH-mutant astrocytoma[76]. 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[77,78,79]. Alternatively, CDKN2A expression and Rb inactivation demonstrate resistance to palbociclib in cases of glioblastoma multiforme[80]. 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[81,82,83,84].

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[35]. Microsatellite instability (MSI) is defined as a change in the length of a microsatellite in a tumor as compared to normal tissue[36,37]. 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[38]. 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[39]. 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)[39]. Tumors classified as MSI-L are often phenotypically indistinguishable from MSS tumors and tend to be grouped with MSS[40,41,42,43,44]. 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[37]. LS is associated with an increased risk of developing colorectal cancer, as well as other cancers, including endometrial and stomach cancer[36,37,41,45].

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[36,37,46,47]. 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[46,47].

Potential relevance: Anti-PD-1 immune checkpoint inhibitors including pembrolizumab[48] (2014) and nivolumab[49] (2015) are approved for patients with MSI-H or dMMR colorectal cancer who have progressed following chemotherapy. Pembrolizumab[48] 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[48]. Dostarlimab[50] (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[42,51]. The cytotoxic T-lymphocyte antigen 4 (CTLA-4) blocking antibody, ipilimumab[52] (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[42,53,54]. 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[54]. 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[55,56]. However, checkpoint blockade with the addition of chemotherapy or targeted therapies have demonstrated response in MSS or pMMR cancers[55,56].

Biomarker Descriptions (continued)

HLA-B deletion

major histocompatibility complex, class I, B

Background: The HLA-B gene encodes the major histocompatibility complex, class I, B[1]. MHC (major histocompatibility complex) class I molecules are located on the cell surface of nucleated cells and present antigens from within the cell for recognition by cytotoxic T cells[2]. MHC class I molecules are heterodimers composed of two polypeptide chains, α and B2M[3]. 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[4,5,6]. Downregulation of MHC class I promotes tumor evasion of the immune system, suggesting a tumor suppressor role for HLA-B[7].

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[8,9]. Biallelic loss of HLA-B is observed in 5% of DLBCL[8,9].

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

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2025-05-14. For the most up-to-date information, search www.fda.gov.

TPM3::ROS1 fusion

taletrectinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Supporting Statement:
The FDA has granted Breakthrough Therapy designation (BTD) to the ROS-1 inhibitor, taletrectinib, for the treatment of adult patients with advanced or metastatic ROS1-positive non-small cell lung cancer (NSCLC) who have not been previously treated with ROS1 tyrosine kinase inhibitors or crizotinib.

Reference:

https://www.anhearttherapeutics.com/news/press-releases/080322/

zidesamtinib

Cancer type: Non-Small Cell Lung Cancer **Variant class:** ROS1 fusion

Supporting Statement:
The FDA has granted Breakthrough Therapy designation to the brain-penetrant ROS1-selective tyrosine kinase inhibitor (TKI), zidesamtinib (NVL-520), for the treatment of patients with ROS1-positive metastatic non-small cell lung cancer (NSCLC) who have been previously treated with two or more ROS1 TKIs.

Reference:

https://investors.nuvalent.com/2024-02-27-Nuvalent-Receives-U-S-FDA-Breakthrough-Therapy-Designation-for-NVL-520

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

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

Genes Assayed for the Detection of Copy Number Variations

ABCB1, ABL1, ABL2, ABRAXAS1, ACVR1B, ACVR2A, ADAMTS12, ADAMTS2, AKT1, AKT2, AKT3, ALK, AMER1, APC, AR, ARAF, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASXL1, ASXL2, ATM, ATR, ATRX, AURKA, AURKC, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BCL2, BCL2L12, BCL6, BCOR, BLM, BMPR2, BRAF, BRCA1, BRCA2, BRIP1, CARD11, CASP8, CBFB, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD276, CDC73, CDH1, CDH10, CDK12, CDK4, CDK6, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CDKN2C, CHD4, CHEK1, CHEK2, CIC, CREBBP, CSMD3, CTCF, CTLA4, CTNND2, CUL3, CUL4A, CUL4B, CYLD, CYP2C9, DAXX, DDR1, DDR2, DDX3X, DICER1, DNMT3A, DOCK3, DPYD, DSC1, DSC3, EGFR, EIF1AX, ELF3, EMSY, ENO1, EP300, EPCAM, EPHA2, ERAP1, ERAP2, ERBB2, ERBB3, ERBB4, ERCC2, ERCC4,

Genes Assayed (continued)

Genes Assayed for the Detection of Copy Number Variations (continued)

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

TPM3::ROS1 fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
entrectinib	●	◑	●	●	● (II/III)
crizotinib	●	◑	●	●	● (II)
repotrectinib	●	●	●	●	● (II)
lorlatinib	✖	●	✖	✖	✖

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

Relevant Therapy Summary (continued)

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

TPM3::ROS1 fusion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
entrectinib, crizotinib	✖	✖	✖	✖	● (III)
repotrectinib, crizotinib	✖	✖	✖	✖	● (III)
sacituzumab tirumotecan	✖	✖	✖	✖	● (III)
taletrectinib, crizotinib	✖	✖	✖	✖	● (III)
targeted therapy	✖	✖	✖	✖	● (III)
cabozantinib	✖	✖	✖	✖	● (II)
ceritinib	✖	✖	✖	✖	● (II)
ICP-723	✖	✖	✖	✖	● (II)
sacituzumab govitecan	✖	✖	✖	✖	● (II)
amivantamab, lorlatinib, entrectinib	✖	✖	✖	✖	● (I/II)
benmelstobart, catequentinib	✖	✖	✖	✖	● (I/II)
furetinib	✖	✖	✖	✖	● (I/II)
XZP-5955	✖	✖	✖	✖	● (I/II)
zidesamtinib	✖	✖	✖	✖	● (I/II)
APG-2449	✖	✖	✖	✖	● (I)
HG 030	✖	✖	✖	✖	● (I)
JYP-0322	✖	✖	✖	✖	● (I)
LZ-001	✖	✖	✖	✖	● (I)
talazoparib, crizotinib	✖	✖	✖	✖	● (I)

ARID1A p.(Q548*) c.1642C>T

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

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

HRR Details

Gene/Genomic Alteration	Finding
LOH percentage	***18.07%***
Not Detected	***Not Applicable***

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

Thermo Fisher Scientific's Ion Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.1.1 data version 2025.06(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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