GENOMIC® TESTING COOPERATIVE

25371 Commercentre Drive, Lake Forest, CA 92630
Tel: 1-866-484-8870 www.genomictestingcooperative.com
CLIA #: 05D2111917 CAP #: 9441574

# Liquid Trace Solid Tumor

| | | | |
|---|---|---|---|
| Patient Name: | | Ordering Physician: | |
| Date of Birth: | | Physician ID: | |
| Gender (M/F): | | Accession #: | |
| Client: | | Specimen Type: | CSF |
| Case #: | | Specimen ID: | |
| Body Site: | | | |

| | | | |
|---|---|---|---|
| MRN: | | Indication for Testing: | |
| Collected Date: | | | |
| Received Date: | | Tumor Type: | |
| Reported Date: | | Stage: | |

## Detected Genomic Alterations

| Level 1 (FDA-Approved) | Level 2 (Standard of Care) | Level 3 (Clinical Evidence) | Level 4 (Biological Evidence) | Other |
|---|---|---|---|---|
| ERBB2 (exon 20 insertion) | Tumor Mutation Burden Low: 3 Mut/Mb | TP53, PPM1D (2 mutations) | BCORL1, MYCN, KMT2C, ACVR1 | Autosomal chromosomes show : 1p-, 1q+, +2, 5p+, +7, +8, 9p-(Bi-allelic deletion of CDKN2A/B), 9q+, 10q-, +17, +19, +20, +21. |

## Results Summary

- **-Mutations in ERBB2, BCORL1, MYCN, TP53, PPM1D (2 mutations), KMT2C, and ACVR1 genes**
  **-Tumor Mutation Burden Low: 3 Mut/Mb**
  **-No evidence of EGFR, KRAS, BRAF, MET, ALK, IDH1/2, H3 K27M, or PTEN mutations**
  **-EBV viral RNA: Not detected**
  **-HPV viral RNA: Not detected**
  **-TTV viral RNA: Not detected**
  **-HLA Genotyping:**
  **-HLA-A: A*24:02-A*24:02**
  **-HLA-B: B*07:02-B*27:05**
  **-HLA-C: C*01:02-C*07:02**
  **-Autosomal chromosomes show : 1p-, 1q+, +2, 5p+, +7, +8, 9p-(Bi-allelic deletion of CDKN2A/B), 9q+, 10q-, +17, +19, +20, +21.**
  **-Increased Keratin mRNA**
  **-Increased ERBB2 mRNA**

  -These findings are consistent with the presence of solid tumor DNA/RNA with markedly high tumor burden.

-ERBB2 exon 20 insertions suggests response to mobocertinib and amivantamab and trastuzumab deruxtecan.

-TP53 mutation suggests possible response to eprenetapopt (APR-246), Aurora kinase A and Wee1 inhibitors.

**See quantitative presentation of mutations at the end of the report.**

| Tumor Heterogeneity |
|---|
| There is a dominant abnormal clone with ERBB2 mutation. The BCORL1 mutation is detected in a subclone. There are abnormal low-level clones with MYCN, TP53, PPM1D (2 mutations), KMT2C, and ACVR1 mutations. |

| Expression | |
|---|---|
| Increased Keratin mRNA | Increased ERBB2 mRNA |

| Diagnostic Implications | |
|---|---|
| ERBB2, BCORL1, MYCN, TP53, PPM1D (2 mutations), KMT2C, ACVR1 | These findings suggest the presence of solid tumor DNA/RNA (see results summary). |

| Relevant Alteration Associated with Resistance |
|---|
| TP53 mutation is associated with resistance to therapy. |
| PPM1D mutations may confer resistance to chemotherapy |

| Levels 2, 3 & 4 (Standard of Care and Clinical/Biological Evidence) | |
|---|---|
| ERBB2 - exon 20 | HER2-targeting tyrosine kinase inhibitor |
| TP53 | Aurora kinase A inhibitors, Wee1 inhibitors, Chk1 inhibitors, kevetrin, APR-246, nutlins, gene therapy |
| PPM1D | PPM1D inhibitors |

| Relevant Genes with NO Alteration | | |
|---|---|---|
| No evidence of mutation in KRAS, NRAS, EGFR, BRAF, or BRCA 1/2 | No specific mutation in DPYD gene, associated with enzymatic deficiency | No evidence of METex14 skipping or EGFRvIII |

## Test Description:

This is a comprehensive molecular profile which uses next generation sequencing (NGS) to identify molecular abnormalities, including single nucleotide variants (SNVs), insertions/deletions (indels), copy number variants (CNVs), tumor mutation burden (TMB), fusions, B- and T-cell clonality, and viruses (HPV, EBV, and TTV), in cell-free (cf) DNA of 302 genes and cfRNA in greater than 1600 genes implicated in solid tumors. Whenever possible, clinical relevance and implications of detected abnormalities are described below.

## Biological relevance of detected Alterations

- ERBB2. This gene encodes a member of the epidermal growth factor (EGF) receptor family of receptor tyrosine kinases. This protein has no ligand binding domain of its own and therefore cannot bind growth factors. However, it does bind tightly to other ligand-bound EGF receptor family members to form a heterodimer, stabilizing ligand binding and enhancing kinase-mediated activation of downstream signalling pathways, such as those involving mitogen-activated protein kinase and phosphatidylinositol-3 kinase. Allelic variations at amino acid positions 654 and 655 of isoform a (positions 624 and 625 of isoform b) have been reported, with the most common allele, Ile654/Ile655, shown here. Amplification and/or overexpression of this gene has been reported in numerous cancers, including breast and ovarian tumors. Alternative splicing results in several additional transcript variants, some encoding different isoforms and others that have not been fully characterized. [provided by RefSeq, Jul 2008]

- BCORL1. The protein encoded by this gene is a transcriptional corepressor that is found tethered to promoter regions by DNA-binding proteins. The encoded protein can interact with several different class II histone deacetylases to repress transcription. Two transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, May 2010]

- MYCN. This gene is a member of the MYC family and encodes a protein with a basic helix-loop-helix (bHLH) domain. This protein is located in the nucleus and must dimerize with another bHLH protein in order to bind DNA. Amplification of this gene is associated with a variety of tumors, most notably neuroblastomas. Multiple alternatively spliced transcript variants encoding different isoforms have been found for this gene. [provided by RefSeq, Jun 2014]

- TP53. This gene encodes a tumor suppressor protein containing transcriptional activation, DNA binding, and oligomerization domains. The encoded protein responds to diverse cellular stresses to regulate expression of target genes, thereby inducing cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Mutations in this gene are associated with a variety of human cancers, including hereditary cancers such as Li-Fraumeni syndrome. Alternative splicing of this gene and the use of alternate promoters result in multiple transcript variants and isoforms. Additional isoforms have also been shown to result from the use of alternate translation initiation codons from identical transcript variants (PMIDs: 12032546, 20937277). [provided by RefSeq, Dec 2016]

- PPM1D. The protein encoded by this gene is a member of the PP2C family of Ser/Thr protein phosphatases. PP2C family members are known to be negative regulators of cell stress response pathways. The expression of this gene is induced in a p53-dependent manner in response to various environmental stresses. While being induced by tumor suppressor protein TP53/p53, this phosphatase negatively regulates the activity of p38 MAP kinase, MAPK/p38, through which it reduces the phosphorylation of p53, and in turn suppresses p53-mediated transcription and apoptosis. This phosphatase thus mediates a feedback regulation of p38-p53 signaling that contributes to growth inhibition and the suppression of stress induced apoptosis. This gene is located in a chromosomal region known to be amplified in breast cancer. The amplification of this gene has been detected in both breast cancer cell line and primary breast tumors, which suggests a role of this gene in cancer development. [provided by RefSeq, Jul 2008]

- KMT2C. This gene is a member of the myeloid/lymphoid or mixed-lineage leukemia (MLL) family and encodes a nuclear protein with an AT hook DNA-binding domain, a DHHC-type zinc finger, six PHD-type zinc fingers, a SET domain, a post-SET domain and a RING-type zinc finger. This protein is a member of the ASC-2/NCOA6 complex (ASCOM), which possesses histone methylation activity and is involved in transcriptional coactivation. [provided by RefSeq, Jul 2008]

- ACVR1. Activins are dimeric growth and differentiation factors which belong to the transforming growth factor-beta (TGF-beta) superfamily of structurally related signaling proteins. Activins signal through a heteromeric complex of receptor serine kinases which include at least two type I ( I and IB) and two type II (II and IIB) receptors. These receptors are all transmembrane proteins, composed of a ligand-binding extracellular domain with cysteine-rich region, a transmembrane domain, and a cytoplasmic domain with predicted serine/threonine specificity Type I receptors are essential for signaling; and type II receptors are required for binding ligands and for expression of type I receptors. Type I and II receptors form a stable complex after ligand binding, resulting in phosphorylation of type I receptors by type II receptors. This gene encodes activin A type I receptor which signals a particular transcriptional response in concert with activin type II receptors. Mutations in this gene are associated with fibrodysplasia ossificans progressive. [provided by RefSeq, Jul 2008]

## Drug Information

### Poziotinib

Poziotinib, previously known as HM781-36B, is a covalent, irreversible tyrosine kinase inhibitor targeting EGFR and HER2 with exon 20 insertion mutations.

### APR-246

APR-246 is a first-in-class agent targeting mutant p53. In vitro and in vivo preclinical models have demonstrated that APR-246 has excellent efficacy in OC (both adenocarcinoma and squamous cell carcinoma) and potently synergises with chemotherapies used in the treatment of OC, restoring sensitivity to chemotherapy-resistant tumours. An initial phase I clinical trial has shown APR-246 to be safe in humans and early results from a currently running phase Ib/II trial of APR-246 with carboplatin and liposomal doxorubicin in ovarian cancer have been promising. Together, these data provide a strong rationale for investigating the efficacy of APR-246 in OC.

APR-246 has been used in trials studying the treatment of Prostatic Neoplasms, Hematologic Neoplasms, and Platinum Sensitive Recurrent High-grade Serous Ovarian Cancer With Mutated p53.

APR-246 is an analogue of PRIMA-1, which modifies the core domain of mutant p53, resulting in restoration of wild-type p53 conformation and reactivation of normal p53 function, leading to increased cell cycle arrest and tumor cell death (PMID: 20498645).

## Potential Clinical Trials

| Trial URL | Status | Title | Disease | Drug | Sites |
|---|---|---|---|---|---|
| https://clinicaltrials.gov/study/NCT05546268 | Recruiting | A Phase 1/2 Study of Oral MRT-2359 in Patients With MYC-Driven and Other Selected Solid Tumors Including Lung Cancer | Non-small Cell Lung Cancer | Oral MRT-2359 | Sarah Cannon Research Institute, Lake Mary, Florida 32746<br>Indiana University, Bloomington, Indiana 46202<br>Dana-Farber Cancer Institute, Boston, Massachusetts 02215 |
| https://clinicaltrials.gov/study/NCT05650879 | Recruiting | A Phase 1a/1b Study of ELVN-002 for the Treatment of Patients With HER2 Mutant Non-Small Cell Lung Cancer | HER2 Mutant Non-small Cell Lung Cancer | ELVN-002, Fam-Trastuzumab Deruxtecan-Nxki, Trastuzumab emtansine | Advent Health Orlando, Orlando, Florida 32804<br>BRCR Medical Center Inc, Plantation, Florida 33322<br>NEXT/Virginia Cancer Specialists, Fairfax, Virginia 22031 |
| https://clinicaltrials.gov/study/NCT06253871 | Recruiting | A Phase 1/1b Study of IAM1363 in Patients with Advanced Cancers Harboring HER2 Alterations | HER2 Mutant Non-small Cell Lung Cancer | IAM1363 | Comprehensive Hematology Oncology, St. Petersburg, Florida 33709<br>University of Michigan, Ann Arbor, Michigan 48109<br>SCRI Oncology Partners, Nashville, Tennessee 37203 |

## Detailed Results

| Single Nucleotide Variant (SNV) and Insertions-Deletions (INDELS) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Gene name | Hgvsp | Hgvsc | Amino acids | Codons | Consequence | Allele frequency | Read depth | Predicted effect on protein |
| ERBB2 | NP_004439.2:p.Tyr772_Ala775dup | NM_004448.2:c.2313_2324dupATACGTGATGGC | -/AYVM | -/GCATACGTGATG | inframe_insertion | 75.33 | 531 | 0 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| BCORL1 | NP_068765.3:p.Ser1246ProfsTer14 | NM_021946.4:c.3736_3749delAGCCAGGAAGTCTT | SQEVF/X | AGCCAGGAAGTCTTc/c | frameshift_variant | 50.46 | 329 | 0 |
| MYCN | NP_005369.2:p.Asp376_Ser377dup | NM_005378.4:c.1125_1130dupTGACTC | N/NSD | aac/aACTCTGac | inframe_insertion | 0.94 | 638 | 0 |
| TP53 | NP_000537.3:p.Cys238Tyr | NM_000546.5:c.713G>A | C/Y | tGt/tAt | missense_variant | 0.89 | 449 | deleterious (0) |
| PPM1D | NP_003611.1:p.Cys478TrpfsTer3 | NM_003620.3:c.1433dupG | C/WX | tgc/tGgc | frameshift_variant | 0.7 | 853 | 0 |
| PPM1D | NP_003611.1:p.Ser468Ter | NM_003620.3:c.1403C>G | S/* | tCa/tGa | stop_gained | 0.49 | 812 | 0 |
| KMT2C | NP_733751.2:p.Gly908Asp | NM_170606.2:c.2723G>A | G/D | gGc/gAc | missense_variant | 0.47 | 850 | 0 |
| ACVR1 (RNA) | NP_001104537.1:p.Arg206His | NM_001111067.2:c.617G>A | R/H | cGc/cAc | missense_variant | 34.86 | 109 | deleterious (0) |

## Methodology and Test Background

This is a next generation sequencing (NGS) test that analyzes cfDNA in 302 genes and cfRNA in >1600 genes for abnormalities that are reported to be altered in various types of solid tumors. For cases with detectable circulating solid tumor DNA, tumor mutation burden (TMB) is reported. The assay also detects several viruses that are important in oncology, including EBV, HPV and TTV. TTV (torque teno virus) was first discovered in a patient with non-A-E hepatitis and is now regarded as a part of the human virome. In general, TTV does not cause pathology in immunocompetent individuals. TTV is considered as a marker of immune competence in patients with immunological impairment and inflammatory disorders. High TTV load is associated with increased risk of infection. In patients with organ transplant, low TTV load is associated with an increased risk of rejection.

Nucleic acid is isolated from peripheral blood plasma. Performance of the assays may vary depending on the quantity and quality of nucleic acid, sample preparation and sample age. Testing is performed using massive parallel sequencing of the coding DNA of the listed genes. This includes sequencing of all the exons as well as approximately 50 nucleotides at the 5' and 3' ends of each coding exon to detect splice site abnormalities. The TERT promoter region, including the hotspots at -124 and -146 bp, is also covered. Our cfDNA sequencing method has a sensitivity of 0.1% for detecting hot spot mutations, 0.5% for detecting single nucleotide variants (SNVs) and 1% for small (<60 bp) insertions/ deletions (indels). Known hot spots in specific genes such as IDH1/2, NRAS, and KRAS are reported at levels of 0.01% and higher when both cfRNA and cfDNA results are combined. Significant gene amplification and deletion (copy number variants) are also reported. TMB is calculated and cut-off points were determined based on comparison with tissue samples obtained from the same patient. Using cut-off of 6 mut/Mb, 17% of cases called as negative by cfDNA are false negative (FN). However, cases with ≤3 show only 6% FN. Intermediate cases (TMB between 6 and 9 mut/Mb) show 51% false positivity. Positive cases (TMB ≥9 Mut/Mb) show only 7% false positive. Cases without circulating solid tumor DNA are reported as "unable to evaluate" for TMB. Targeted RNA NGS is performed by hybrid capture and duplicates are excluded for levels measurements. The Universal Human Reference (UHR) RNA is used as control. All detected fusion transcripts are reported. While the major focus of the RNA analysis is the detection of fusion mRNA, mutations in the expressed RNA of the analyzed genes, HLA class I genotyping, and Epstein-Barr virus (EBV), human papillomavirus (HPV) and torque teno virus (TTV) viral RNA are also analyzed and reported. B- and T-cell clonality will be reported, if clonal or clinically relevant. The sensitivity of this assay in detecting fusion mRNA is between 5% and 10%. This test specifically covers translocations that lead to the expression of fusion RNA. Translocations that lead to deregulation of expression can be addressed by this test if compared to the expression proper normal control. Since the clinical relevance of the RNA expression level of most of the genes is not characterized at this time, only a few specific genes will be commented on when abnormalities are detected. CD274 (PD-L1) mRNA levels are reported when they are significantly elevated.

Based on our validation study, the following exonic regions of the genes listed below are not covered appropriately <100 X coverage and sequencing by NGS may not be reliable in these regions. The poor coverage is primarily due to the inherent difficulty in obtaining adequate sequencing coverage in regions with high GC content. No well-

characterized hotspots are present in these regions. RAD51 NM_133487 chr15:40994004-40994124, BRCA1 NM_007300 chr17:41231351-41231416, FUBP1 NM_003902 chr1:78435609-78435699, CBLB NM_170662 chr3:105420938-105421303, TERT NM_198253 chr5:1295183-1295250, ARID1B NM_017519 chr6:157098715-157100605, CUX1 NM_001202543 chr7:101740644-101740781, KMT2C NM_170606 chr7:151891314-151891346 and 151935792-151935911, GALNT12 NM_024642 chr9:101569952-101570351, ATM NM_000051 chr11:108164040-108164204, CDK17 NM_001170464 chr12:96679880-96679926, RB1 NM_000321 chr13:48954189-48954220, SETBP1 NM_015559 chr18:42643044-42643692, KMT2B NM_014727 chr19:36208921-36209283, AR NM_000044 chrX:66764889-66766604, STAG2 NM_001042749 chrX:123200025-123200112.

**The table below may contain a partial list of the tested DNA genes. For a complete list, please go to:**
https://genomictestingcooperative.com/genomic-tests/liquid-trace-solid-tumor/ (click the DNA tab)

**For a complete list of tested RNA genes (Fusions/Expression), please go to:**
https://genomictestingcooperative.com/genomic-tests/liquid-trace-solid-tumor/ (click the RNA tab)

## Tested genes

| Genes Tested for Abnormalities in Coding Sequence | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ABL1 | ATRX | BRAF | CDK12 | CUX1 | EPHA5 | FGF4 | GNAQ | IL7R | MAP2K1 | MSH3 | NPM1 | PIM1 | RAD21 | SDHB | SRSF2 | TRAF3 |
| ABRAXAS1 | AURKA | BRCA1 | CDK4 | CXCR4 | ERBB2 | FGF6 | GNAS | INHBA | MAP2K2 | MSH6 | NRAS | PLCG1 | RAD50 | SDHC | STAG2 | TSC1 |
| ACVR1B | AURKB | BRCA2 | CDK6 | CYLD | ERBB3 | FGFR1 | GNB1 | IRF4 | MAP2K4 | MTOR | NSD1 | PMS1 | RAD51 | SDHD | STAT3 | TSC2 |
| AKT1 | AURKC | BRIP1 | CDKN1B | DAXX | ERBB4 | FGFR2 | GREM1 | JAK1 | MAP3K1 | MUTYH | NSD2 (WHSC1) | PMS2 | RAD51C | SETBP1 | STAT5B | TSHR |
| AKT2 | AXIN1 | BTK | CDKN2A | DDR2 | ERG | FGFR3 | GRIN2A | JAK2 | MAP3K14 | MYC | NTHL1 | POLD1 | RAD51D | SETD2 | STK11 | U2AF1 |
| AKT3 | AXIN2 | CALR | CDKN2B | DDX41 | ESR1 | FGFR4 | H3-3A (H3F3A) | JAK3 | MAPK1 | MYCL | NTRK1 | POLE | RAF1 | SF3B1 | SUFU | U2AF2 |
| ALK | B2M | CARD11 | CDKN2C | DICER1 | ETNK1 | FH | H3C2 | KAT6A | MCL1 | MYCN | NTRK2 | POT1 | RB1 | SMAD2 | SUZ12 | UBA1 |
| AMER1 | BAP1 | CBL | CEBPA | DNM2 | ETV6 | FLCN | HGF | KDM5C | MDM2 | MYD88 | NTRK3 | PPM1D | RET | SMAD4 | TAL1 | VHL |
| ANKRD26 | BARD1 | CBLB | CHEK1 | DNMT3A | EXO1 | FLT3 | HNF1A | KDM6A | MDM4 | NBN | PAK3 | PPP2R1A | RHEB | SMARCA4 | TCF3 | WT1 |
| APC | BCL2 | CBLC | CHEK2 | DOT1L | EZH2 | FLT4 | HOXB13 | KDR | MED12 | NF1 | PALB2 | PRDM1 | RHOA | SMARCB1 | TENT5C (FAM46C) | XPO1 |
| AR | BCL2L1 | CCND1 | CIC | EED | FANCA | FOXL2 | HRAS | KEAP1 | MEF2B | NF2 | PAX5 | PRKAR1A | RIT1 | SMC1A | TERC | XRCC2 |
| ARAF | BCL6 | CCND3 | CREBBP | EGFR | FANCC | FUBP1 | HSP90AA1 | KIT | MEN1 | NFE2 | PBRM1 | PRKDC | RNF43 | SMC3 | TERT | XRCC3 |
| ARID1A | BCOR | CCNE1 | CRLF2 | EGLN1 | FANCD2 | GALNT12 | ID3 | KMT2A | MET | NFE2L2 | PDGFRA | PRPF8 | ROS1 | SMO | TET2 | ZNF217 |
| ARID1B | BCORL1 | CD274 | CSF1R | ELANE | FANCE | GATA1 | IDH1 | KMT2B | MITF | NFKBIA | PDGFRB | PRSS1 | RUNX1 | SOCS1 | TGFBR2 | ZRSR2 |
| ARID2 | BCR | CD79A | CSF3R | EP300 | FANCF | GATA2 | IDH2 | KMT2C | MLH1 | NKX2-1 | PHF6 | PTCH1 | SAMD9 | SOX2 | TMEM127 | - |
| ASXL1 | BIRC3 | CD79B | CTCF | EPAS1 | FANCG | GATA3 | IGF1R | KMT2D | MPL | NOTCH1 | PIK3CA | PTEN | SAMD9L | SOX9 | TNFAIP3 | - |
| ATM | BLM | CDC73 | CTNNA1 | EPCAM | FAS | GEN1 | IKZF1 | KRAS | MRE11 | NOTCH2 | PIK3R1 | PTPN11 | SDHA | SPOP | TNFRSF14 | - |
| ATR | BMPR1A | CDH1 | CTNNB1 | EPHA3 | FBXW7 | GNA11 | IKZF3 | LRP1B | MSH2 | NOTCH3 | PIK3R2 | RAC1 | SDHAF2 | SRC | TP53 | - |

## RNA Fusions/Expression

| Fusion/Expression | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ABL1 | BCL6 | CD274 (PD-L1) | EGFR | EWSR1 | FLI1 | IKZF3 | MAP3K1 | NRG1 | NUP98 | PML | RET | SS18 | THADA |
| AKT3 | BRAF | CIC | ERG | FGFR1 | FOXO1 | JAK2 | MECOM | NTRK1 | PAX8 | PPARG | RHOA | STAT6 | TMPRSS2 |
| ALK | CAMTA1 | CREB1 | ETS1 | FGFR2 | FUS | KIAA1549 | MYB | NTRK2 | PDGFRA | PRKACA | ROS1 | TAL1 | YAP1 |
| AR | CBFB | CREBBP | ETV1 | FGFR3 | GLI1 | KMT2A | MYC | NTRK3 | PDGFRB | RAF1 | RUNX1 | TCF3 | YWHAE |
| BCL2 | CCND1 | ERBB2 | ETV6 | FIP1L1 | HMGA2 | MAML2 | NOTCH1 | NUP214 | PICALM | RARA | RUNX1T1 | TFG | ZFTA |

## Reference

1. Targeting HER2 genomic alterations in non-small cell lung cancer. Zeng J, Ma W, Young RB, Li T. J Natl Cancer Cent. 2021 May 3;1(2):58-73. doi: 10.1016/j.jncc.2021.04.001. eCollection 2021 Jun. PMID: 39035769.

2. Top advances of the year: Targeted therapy for lung cancer. Makarem M, J nne PA. Cancer. 2024 Oct 1;130(19):3239-3250. doi: 10.1002/cncr.35423. Epub 2024 Jun 21. PMID: 39031586.

4. Management of HER2 alterations in non-small cell lung cancer - The past, present, and future. N tzinger J, Bum Lee J, Li Low J, Ling Chia P, Talisa Wijaya S, Chul Cho B, Min Lim S, Soo RA. Lung Cancer. 2023 Dec;186:107385. doi: 10.1016/j.lungcan.2023.107385. Epub 2023 Sep 28. PMID: 37813015.

5. Trastuzumab Deruxtecan-Induced Interstitial Lung Disease/Pneumonitis in ERBB2-Positive Advanced Solid Malignancies: A Systematic Review. Abuhelwa Z, Alloghbi A, Alqahtani A, Nagasaka M. Drugs. 2022 Jun;82(9):979-987. doi: 10.1007/s40265-022-01736-w. Epub 2022 Jun 27. PMID: 35759121.

## Electronic Signature

# Additional Report Information