

Date of Birth  
**01/01/1990**Sex  
**Male**Physician  
**Test Physician**Institution  
**Test Institution 123456789****TEMPUS | xT**  
648 gene panel**Tumor specimen:**

Lung, left  
 Test Institution Pathology  
 Laboratory S22-123456, A2  
 Collected 02/06/2022  
 Received 02/09/2022  
 Tumor Percentage: 70%

**Normal specimen:**

Blood  
 Collected 02/06/2022  
 Received 02/11/2022

**GENOMIC VARIANTS****Somatic - Potentially Actionable**

 **MET-ALK** Chromosomal rearrangement

Variant Allele Fraction

**Somatic - Biologically Relevant**

 **BAP1** p.Q590\* Stop gain - LOF

57.4% 

 **CDKN2A** Copy number loss

 **CDKN2B** Copy number loss

 **KDM5D** Copy number loss

 **MTAP** Copy number loss

 **MYCN** Copy number gain

**Germline - Pathogenic / Likely Pathogenic**

No germline pathogenic variants were found in the limited set of genes on which we report.

**Pertinent Negatives**

No pathogenic single nucleotide variants, indels, or copy number changes found in:

 **NRAS**  **KIT**  **BRAF**

**IMMUNOTHERAPY MARKERS****Tumor Mutational Burden**

**5.2 m/MB** 83rd percentile

**✓ FDA-APPROVED THERAPIES, CURRENT DIAGNOSIS**

Anti-EGFR MAb

**Cetuximab or Panitumumab**



NCCN, Consensus, Colorectal Cancer



MSK OncoKB, Level 1

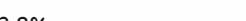
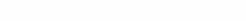
Wild Type: KRAS, NRAS, BRAF

ALK Inhibitor	<b>Alectinib</b>	NCCN, Consensus, Non-Small Cell Lung Cancer MET-ALK Chromosomal rearrangement
ALK/EGFR Inhibitor	<b>Brigatinib</b>	NCCN, Consensus, Non-Small Cell Lung Cancer MET-ALK Chromosomal rearrangement
ALK/ROS1 Inhibitor	<b>Ceritinib</b>	NCCN, Consensus, Non-Small Cell Lung Cancer MET-ALK Chromosomal rearrangement
	<b>Crizotinib</b>	NCCN, Consensus, Non-Small Cell Lung Cancer MET-ALK Chromosomal rearrangement FDA, Consensus, Anaplastic Large Cell Lymphoma <span style="border: 1px solid black; padding: 0 2px;">Pediatric</span> MET-ALK Chromosomal rearrangement
	<b>Lorlatinib</b>	NCCN, Consensus, Non-Small Cell Lung Cancer MET-ALK Chromosomal rearrangement

We were unable to determine whether treatments on this report were previously prescribed for this patient.

A "Pediatric" tag means that the cited evidence supports use in a pediatric population. Please review the specific evidence to identify the relevant age group of the specific pediatric population.

## VARIANTS OF UNKNOWN SIGNIFICANCE

Somatic	Mutation effect	Variant allele fraction
POF1B	c.430C>T p.P144S Missense variant NM_001307940	78.6% 
POLRMT	c.598G>A p.G200R Missense variant NM_005035	75.6% 
KCTD3	c.2425T>G p.S809A Missense variant NM_016121	73.6% 
LRRC31	c.1159+5G>A Splice region variant NM_024727	72.8% 
ADGRV1	c.12793C>T p.P4265S Missense variant NM_032119	72.8% 
C1orf64	c.259G>A p.E87K Missense variant NM_178840	72.7% 
ATP8B3	c.485A>G p.N162S Missense variant NM_138813	71.8% 
GPRASP1	c.2630C>T p.S877F Missense variant NM_001099411	71.7% 
BRINP3	c.1983G>A p.M661I Missense variant NM_199051	71.4% 
HDAC8	c.611C>T p.S204F Missense variant NM_018486	68.8% 
GNA11	c.546_547delinsTT p.VR182VC Missense variant NM_002067	68.3% 

## Assay Description

The Tempus xT(version 4) assay is a custom oncology testing panel consisting of 648 genes with single nucleotide variants, indels and translocations measured by hybrid capture next-generation sequencing (NGS). A complete gene list can be found at the end of this assay description. This assay has 98.2% sensitivity for single nucleotide variants (SNV) above 5% variant allele fraction (VAF), 91.8% sensitivity for indels above 5% VAF and 91.7% sensitivity for reported translocations. The assay has 91.3% sensitivity for copy number alterations for samples with the copy number gain limit of detection (LOD) set as 30% tumor purity and copy number loss at 40% tumor purity. (Certain driver or resistance genes may be reported to lower VAFs when technically possible.)

**Potentially Actionable** alterations are protein-altering variants with an associated therapy based on evidence from the medical literature. **Biologically Relevant** alterations are protein-altering variants that may have functional significance or have been observed in the medical literature but are not associated with a specific therapy in the Tempus knowledge database. **Variants of Unknown Significance (VUSs)** are protein-altering variants exhibiting an unclear effect on function and/or without sufficient evidence to determine their pathogenicity. **Benign variants** are not reported. Variants are identified through aligning the patient's DNA sequence to the human genome reference sequence version hg19 (GRCh37). The clinical summary (first page of the report) shows actionable and biologically relevant somatic variants, and certain pathogenic or likely pathogenic inherited variants that are reported as incidental findings (if a matched normal sample was provided and analyzed). Reportable secondary/incidental findings are limited to genes and variants associated with inherited cancer syndromes.

**Tumor mutational burden (TMB)** measures the quantity of somatic SNVs and indels, of any pathogenicity, including benign, carried in a tumor as the number of protein-altering mutations per million coding base pairs. TMB is calculated at the time of initial report delivery. Accordingly, the TMB calculation is based upon (a) both the tumor and normal sample if Tempus had analyzed both at the time of the initial report, or (b) the tumor sample only if no normal sample had been analyzed at the time of the initial report. Please note that tumor only calculations are not updated or amended even if a normal sample is subsequently analyzed. Studies have shown that tumors with higher TMB have an increased likelihood of response to immunotherapy [1, 2].

**Microsatellite instability (MSI)** refers to hypermutability caused by genetic or acquired defects in the DNA mismatch repair pathway. MSI status is divided into **MSI-high (MSI-H)** tumors, which have changes in microsatellite repeat lengths due to defective DNA mismatch repair activity.

**Microsatellite stable (MSS)** tumors do not have detectable defects in DNA mismatch repair. **Microsatellite equivocal (MSE)** tumors have an intermediate phenotype which cannot be clearly classified as MSI-H or MSS based on the statistical cutoff used to define those categories. If MSI status will affect clinical management, immunohistochemical staining for DNA mismatch repair proteins, or another method of ascertaining MSI status, is recommended.

The Tempus 2nd generation RNA whole-transcriptome assay (RS.v2) uses IDT xGen Exome Research Panel v2 probe set as backbone, which consists of >415K individually synthesized probes and spans 34 Mb target region (19,433 genes) of the human genome. Additional Tempus-specific custom spike-ins probes are added to enhance target region detection (e.g., fusion and viral probes). When whole transcriptome RNA-Seq is performed, expressed fusion transcripts from rearranged genes specifically targeted by the assay will be detected. In addition to this, expressed fusion transcripts from rearranged genes not targeted by the assay may also be detected. A list of targeted fusion transcripts can be made available upon request. The fusion transcript detection bioinformatics pipeline identifies and analyzes the positions of breakpoint spanning reads and split paired-end reads. Non-canonical fusion transcripts may be reported at the discretion of the medical director. This assay has >99% sensitivity for targeted fusion and 97% sensitivity for untargeted fusions.

1. Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. <https://www.ncbi.nlm.nih.gov/pubmed/29658845>

2. Cancer immunology. Mutational landscape determines sensitivity to PD-1 blockade in non-small cell lung cancer.

<https://www.ncbi.nlm.nih.gov/pubmed/25765070>

## Gene List

### A-B

ABCB1, ABCC3, ABL1, ABL2, ABRAVAS1, ACTA2, ACVR1 (ALK2), ACVR1B, AGO1, AJUBA, AKT1, AKT2, AKT3, ALK, AMER1, APC, APLNR, APOB, AR, ARAF, ARHGAP26, ARHGAP35, ARID1A, ARID1B, ARID2, ARID5B, ASNS, ASPSCR1, ASXL1, ATIC, ATM, ATP7B, ATR, ATRX, AURKA, AURKB, AXIN1, AXIN2, AXL, B2M, BAP1, BARD1, BCL10, BCL11B, BCL2, BCL2L1, BCL2L11, BCL6, BCL7A, BCLAF1, BCOR, BCORL1, BCR, BIRC3, BLM, BMPR1A, BRAF, BRCA1, BRCA2, BRD4, BRIP1, BTG1, BTK, BUB1B

### C-D

C11orf65, C3orf70, C8orf34, CALR, CARD11, CARM1, CASP8, CASR, CFB, CBL, CBLB, CBLC, CBR3, CCDC6, CCND1, CCND2, CCND3, CCNE1, CD19, CD22, CD274 (PD-L1), CD40, CD70, CD79A, CD79B, CDC73, CDH1, CDK12, CDK4, CDK6, CDK8, CDKN1A, CDKN1B, CDKN1C, CDKN2A, CDKN2B, CDKN2C, CEBPA, CEP57, CFTR, CHD2, CHD4, CHD7, CHEK1, CHEK2, CIC, CIITA, CKS1B, CREBBP, CRKL, CRLF2, CSF1R, CSF3R, CTC1, CTCF, CTLA4, CTNNA1, CTNNB1, CTRC, CUL1, CUL3, CUL4A, CUL4B, CUX1, CXCR4, CYLD, CYP1B1, CYP2D6, CYP3A5, CYSLTR2, DAXX, DDB2, DDR2, DDX3X, DICER1, DIRC2, DIS3, DIS3L2, DKC1, DNM2, DNMT3A, DOT1L, DPYD, DYNC2H1

**Assay Description (continued)****E-F**

EBF1, ECT2L, EGF, EGFR, EGLN1, EIF1AX, ELF3, ELOC (TCEB1), EMSY, ENG, EP300, EPCAM, EPHA2, EPHA7, EPHB1, EPHB2, EPOR, ERBB2 (HER2), ERBB3, ERBB4, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERCC6, ERG, ERRFI1, ESR1, ETS1, ETS2, ETV1, ETV4, ETV5, ETV6, EWSR1, EZH2, FAM46C, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FAS, FAT1, FBXO11, FBXW7, FGCR2A, FGCR3A, FDPS, FGF1, FGF10, FGF14, FGF2, FGF23, FGF3, FGF4, FGF5, FGF6, FGF7, FGF8, FGF9, FGFR1, FGFR2, FGFR3, FGFR4, FH, FHIT, FLCN, FLT1, FLT3, FLT4, FNTB, FOXA1, FOXL2, FOXO1, FOXO3, FOXP1, FOXQ1, FR52, FUBP1, FUS

**G-H**

G6PD, GABRA6, GALNT12, GATA1, GATA2, GATA3, GATA4, GATA6, GEN1, GLI1, GLI2, GNA11, GNA13, GNAQ, GNAS, GPC3, GPS2, GREM1, GRIN2A, GRM3, GSTP1, H19, H3F3A, HAS3, HAVCR2, HDAC1, HDAC2, HDAC4, HGF, HIF1A, HIST1H1E, HIST1H3B, HIST1H4E, HLA-A, HLA-B, HLA-C, HLA-DMA, HLA-DMB, HLA-DOA, HLA-DOB, HLA-DPA1, HLA-DPB1, HLA-DPB2, HLA-DQA1, HLA-DQA2, HLA-DQB1, HLA-DQB2, HLA-DRA, HLA-DRB1, HLA-DRB5, HLA-DRB6, HLA-E, HLA-F, HLA-G, HNF1A, HNF1B, HOXA11, HOXB13, HRAS, HSD11B2, HSD3B1, HSD3B2, HSP90AA1, HSPH1

**I-K**

IDH1, IDH2, IDO1, IFIT1, IFIT2, IFIT3, IFNAR1, IFNAR2, IFNGR1, IFNGR2, IFNL3, IKBKE, IKZF1, IL10RA, IL15, IL2RA, IL6R, IL7R, ING1, INPP4B, IRF1, IRF2, IRF4, IRS2, ITPKB, JAK1, JAK2, JAK3, JUN, KAT6A, KDM5A, KDM5C, KDM5D, KDM6A, KDR, KEAP1, KEL, KIF1B, KIT, KLF4, KLHL6, KLLN, KMT2A, KMT2B, KMT2C, KMT2D, KRAS

**L-M**

L2HGDH, LAG3, LAT51, LCK, LDLR, LEF1, LMNA, LMO1, LRP1B, LYN, LZTR1, MAD2L2, MAF, MAFB, MAGI2, MALT1, MAP2K1, MAP2K2, MAP2K4, MAP3K1, MAP3K7, MAPK1, MAX, MC1R, MCL1, MDM2, MDM4, MED12, MEF2B, MEN1, MET, MGMT, MIB1, MITF, MKI67, MLH1, MLH3, MLLT3, MN1, MPL, MRE11, MS4A1, MSH2, MSH3, MSH6, MTAP, MTHFD2, MTHFR, MTOR, MTRR, MUTYH, MYB, MYC, MYCN, MYD88, MYH11

**N-O**

NBN, NCOR1, NCOR2, NF1, NF2, NFE2L2, NFKBIA, NHP2, NKX2-1, NOP10, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NPM1, NQO1, NRAS, NRG1, NSD1, NSD2, NT5C2, NTHL1, NTRK1, NTRK2, NTRK3, NUDT15, NUP98, OLIG2

**P-Q**

P2RY8, PAK1, PALB2, PALLD, PAX3, PAX5, PAX7, PAX8, PBRM1, PCBP1, PDCD1, PDCD1LG2, PDGFRA, PDGFRB, PDK1, PHF6, PHGDH, PHLPP1, PHLPP2, PHOX2B, PIAS4, PIK3C2B, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R1, PIK3R2, PIM1, PLCG1, PLCG2, PML, PMS1, PMS2, POLD1, POLE, POLH, POLQ, POT1, POU2F2, PPARA, PPARD, PPARG, PPM1D, PPP1R15A, PPP2R1A, PPP2R2A, PPP6C, PRCC, PRDM1, PREX2, PRKAR1A, PRKDC, PRKN, PRSS1, PTCH1, PTCH2, PTEN, PTPN11, PTPN13, PTPN22, PTPRD, PTPRT, QKI

**R-S**

RAC1, RAD21, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD54L, RAF1, RANBP2, RARA, RASA1, RB1, RBM10, RECQL4, RET, RHEB, RHOA, RICTOR, RINT1, RIT1, RNF139, RNF43, ROS1, RPL5, RPS15, RPS6KB1, RPTOR, RRM1, RSF1, RUNX1, RUNX1T1, RXRA, SCG5, SDHA, SDHAF2, SDHB, SDHC, SDHD, SEC23B, SEMA3C, SETBP1, SETD2, SF3B1, SGK1, SH2B3, SHH, SLC26A3, SLC47A2, SLC9A3R1, SLIT2, SLX4, SMAD2, SMAD3, SMAD4, SMARCA1, SMARCA4, SMARCB1, SMARCE1, SMC1A, SMC3, SMO, SOCS1, SOD2, SOX10, SOX2, SOX9, SPEN, SPINK1, SPOP, SPRED1, SRC, SRSF2, STAG2, STAT3, STAT4, STAT5A, STAT5B, STAT6, STK11, SUFU, SUZ12, SYK, SYNE1

**T-U**

TAF1, TANC1, TAP1, TAP2, TARBP2, TBC1D12, TBL1XR1, TBX3, TCF3, TCF7L2, TCL1A, TERT, TET2, TFE3, TFEB, TFEC, TGFBR1, TGFBR2, TIGIT, TMEM127, TMEM173, TMPRSS2, TNF, TNFAIP3, TNFRSF14, TNFRSF17, TNFRSF9, TOP1, TOP2A, TP53, TP63, TPM1, TPMT, TRAF3, TRAF7, TSC1, TSC2, TSHR, TUSC3, TYMS, U2AF1, UBE2T, UGT1A1, UGT1A9, UMPS

**V-Z**

VEGFA, VEGFB, VHL, VSIR, WEE1, WNK1, WNK2, WRN, WT1, XPA, XPC, XPO1, XRCC1, XRCC2, XRCC3, YEATS4, ZFHX3, ZMYM3, ZNF217, ZNF471, ZNF620, ZNF750, ZNRF3, ZRSR2

**Gene Rearrangements Found by DNA Sequencing**

ABL1, ALK, BCR, BRAF, EGFR, ETV6, EWSR1, FGFR2, FGFR3, MYB, NRG1, NTRK1, NTRK2, NTRK3, PAX8, PDGFRA, PML, RARA, RET, ROS1, TFE3, TMPRSS2

**Germline Genes**

APC, ATM, AXIN2, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDKN2A, CEBPA, CHEK2, EGFR, EPCAM, ETV6, FH, FLCN, GATA2, MEN1, MLH1, MSH2, MSH3, MSH6, MUTYH, NBN, NF2, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, RB1, RET, RUNX1, SDHAF2, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, TSC1, TSC2, VHL, WT1

**RNA Fusion Analysis**

RNA transcriptome analysis for fusion detection will be attempted on all samples. If fusions are identified via RNA sequencing, they will be added to the report or issued as an addendum.

## Tempus Disclaimer

The analysis of nucleic acids by next-generation sequencing (NGS) can be affected by multiple factors including formalin-fixation degrading DNA and RNA quality, and low tumor purity limiting sensitivity. Additionally, the chance of detecting genetic alterations may be reduced in regions of the genome which are structurally difficult to sequence, in homologous genes, or due to low complexity regions prone to sequencing error.

Genetic alterations are defined as clinically significant based on peer-reviewed published literature and other authoritative sources such as NCCN guidelines. These references are not comprehensive, therefore clinically unknown findings may occur.

These test results and information contained within the report are current as of the report date. Tempus will not update reports or send notification regarding reclassification of genomic alterations. This test was developed and its performance characteristics determined by Tempus. It has not been cleared or approved by the FDA. The laboratory is CLIA certified to perform high-complexity testing. Any decisions related to patient care and treatment choices should be based on the independent judgment of the treating physician and should take into account all information related to the patient, including without limitation, the patient and family history, direct physical examination and other tests. Tempus is not liable for medical judgment with regards to diagnosis, prognosis or treatment in connection with the test results.

Tempus may report certain germline secondary/incidental findings as part of these test results. The reportable secondary/incidental findings for the genes included on these panels include genes recommended by the ACMG [1], the NCCN, and other published literature and are associated with inherited cancer syndromes. These secondary/incidental findings may or may not be related to the patient's current cancer diagnosis. The clinical significance of any such reported variants are based on germline classification criteria created by the ACMG [2]. Variants that are classified as pathogenic, likely pathogenic, or as a risk allele may be reported. Variants of uncertain significance (VUS), likely benign, and benign variants are not reported. Classifications are provided based on evidence evaluated at the time of reporting. When a variant is detected in both the somatic and germline samples, the variant is reported only under the "germline" section of genomic variants, unless otherwise noted. Tempus does not notify physicians or patients of updated variant classifications.

This is not a stand alone germline test, and as such the rate of false positives and false negatives has not been assessed and certain alterations, such as exon level rearrangements may be missed. Additionally, detection of genetic variation in genes with high homology to other regions of the genome may be decreased or not reliably detected by NGS (including but not limited to these genes: NF1, PMS2, SBDS, and SUZ12) and large insertions and deletions may also not be detected by NGS. Because of these limitations, these germline test results cannot be used to definitively rule out cancer or other genetic predisposition syndromes. Unless Tempus has provided a separate report indicating that a specific germline finding is validated, the incidental germline finding results set forth herein should not be used as a substitute for tests validated to determine genetic risk; additional validated hereditary testing may be recommended for incidental germline findings not validated in a separate report from Tempus.

Results of genetic testing, including the incidental germline findings described above, may have implications for both the patient and family members. Tempus does not provide genetic counseling; however, genetic counseling is strongly suggested, based on the patient's clinical history and/or genetic test results. The ordering physician or the patient is responsible for contacting a genetic counselor to discuss test results.

1. Kalia SS, Adelman K, Bale SJ, Chung WK, Eng C, Evans JP, Herman GE, Hufnagel SB, Klein TE, Korf BR, McKelvey KD, Ormond KE, Richards CS, Vlangos CN, Watson M, Martin CL, Miller DT., Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics. *Genet Med.* 2016 Nov 17. DOI: 10.1038/gim.2016.190.

2. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, Grody WW, Hegde M, Lyon E, Spector E, Voelkerding K, Rehm HL; Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. ACMG Laboratory Quality Assurance Committee. *Genet Med.* 2015 May;17(5):405-24. DOI: 10.1038/gim.2015.30.