Diagnosis
Solitary fibrous tumor

Accession No.

xT

Date of Birth
01/01/1954

Sex
Male

Physician
Raphael Borok

Institution
Precision Diagnostic Laboratory 1966427

TEMPUS | xT 596 Genes

Tumor specimen:
Mediastinum

[redacted]

Notes

RNA expression analysis has been performed and is reported in the Tempus online portal.

GENOMIC VARIANTS

Somatic - Potentially Actionable — Variant Allele Fraction

RB1 Copy number loss

NAB2 - STAT6 Chromosomal rearrangement

Somatic - Biologically Relevant

TERT c.-124C>T Variant - Promoter mutation 47.1%

Germline - Pathogenic / Likely Pathogenic

No matched normal sample was received, therefore germline sequencing was not performed.

IMMUNOTHERAPY MARKERS

Tumor Mutational Burden

1.7 m/MB 25th percentile

Microsatellite Instability Status

Stable | Equivocal | High

FDA-APPROVED THERAPIES, OTHER INDICATIONS

HDAC Inhibitor	**Vorinostat**	RB1 Copy number loss Loss-of-function Preclinical, Retinoblastoma: PMID 18483379

INVESTIGATIONAL THERAPIES

AURK Inhibitor	**LY3295668**	RB1 Copy number loss Loss-of-function Preclinical, Cancer: PMID 30373917
HDAC Inhibitor	**Trichostatin or Entinostat**	RB1 Copy number loss Loss-of-function Preclinical, Retinoblastoma: PMID 18483379

ADDITIONAL INDICATORS

Diagnostic	NAB2-STAT6 Chromosomal rearrangement Consensus, Solitary Fibrous Tumors: NCCN

CLINICAL TRIALS

A Study of LY2606368 (Prexasertib) in Patients With Solid Tumors With Replicative Stress or Homologous Repair Deficiency (NCT02873975)	**Phase II** Boston, MA - 863 mi ✓ **RB1 deletion**
CPI-006 Alone and in Combination With CPI-444 and With Pembrolizumab for Patients With Advanced Cancers (NCT03454451)	**Phase I** Chicago, IL - 17 mi
Phase 1 Study of INBRX-109 in Subjects With Locally Advanced or Metastatic Solid Tumors Including Sarcomas (NCT03715933)	**Phase I** Chicago, IL - 17 mi

VARIANTS OF UNKNOWN SIGNIFICANCE

Somatic	Mutation effect	Variant allele fraction
KMT2D	c.1043G>A p.R348H Missense variant NM_003482	56.3%
APOB	c.5722G>A p.D1908N Missense variant NM_000384	38.9%
TKT	c.1067C>T p.S356L Missense variant NM_001258028	37.3%
CIC	c.5449G>T p.A1817S Missense variant NM_001304815	35.9%
HLA-DPA1	c.221G>A p.W74* Stop gain NM_001242525	31.8%

LOW COVERAGE REGIONS

GFRA2	NOTCH1	PDPK1	TAF1

SOMATIC VARIANT DETAILS - POTENTIALLY ACTIONABLE

RB1 Copy number loss

RB1 encodes the protein pRb that regulates E2F activity in the RB1/E2F pathway, a pathway responsible for the transition from the G1 to the S phase in the cell cycle. Loss of function mutations, copy number loss, epigenetic variation, and underexpression of RB1 are associated with cancer progression.

NAB2 - STAT6 Chromosomal rearrangement

NAB2-STAT6 is a fusion oncoprotein that contains a truncated transcriptional repressor domain of NAB2 fused in-frame to the transcriptional activation domain of STAT6. This fusion results in overexpression of downstream EGR1 target genes and results in tumorigenesis.

TERT c.-124C>T NM_198253 Variant - Promoter mutation VAF: 47.1%

TERT encodes the protein telomerase, the enzyme responsible for maintaining the repeated segments of DNA at the ends of chromosomes called telomeres. Telomeres prevent the degradation of chromosomes during replication. Activating mutations, copy numbers gains, and overexpression of TERT are associated with cancer progression.

Assay Description

The Tempus xT assay is a custom oncology testing panel consisting of 596 genes with single nucleotide variants, indels and translocations measured by hybrid capture next-generation sequencing (NGS). For the complete gene list, see the Tempus website.. The limit of detection of the assay is 5% variant allele fraction (VAF) with sensitivity of 99.1% for single nucleotide variants, 10% VAF with sensitivity of 98.1% for indels and 99.9% sensitivity for translocations. (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 the patient has consented to receive germline findings).

Tumor mutational burden (TMB) measures the quantity of somatic mutations, of any pathogenicity, including benign, carried in a tumor as the number of single nucleotide protein-altering mutations per million base pairs. 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.

When whole transcriptome RNA-Seq is done, expressed fusion transcripts from rearranged genes are detected in an unbiased (non-targeted) fashion. The Tempus RNA whole transcriptome assay uses the IDT xGen Exome Research Panel v1.0 hybridization probes. The fusion transcript detection bioinformatics pipeline analyzes and shows the positions of breakpoint spanning reads and split paired-end reads. This is compared to the Tempus knowledge database of previously-reported fusion transcripts. Non-canonical fusion transcripts may be reported at the discretion of the medical director.

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

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 sequencing errors.

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.

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Tempus Disclaimer (continued)

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.

If the patient has consented to germline reporting, then consistent with the recommendations of the ACMG [1], Tempus reports certain germline secondary/incidental findings. These incidental findings include germline sequencing results associated with serious conditions that may or may not be related to the patient's current cancer diagnosis but are considered medically actionable. The clinical significance of reported variants is based on germline classification criteria created by the ACMG [2].

Since these are incidental findings and not a stand alone germline test, the rate of false negatives has not been assessed and certain mutations, 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 tests results cannot be used to definitively rule out cancer or other genetic predisposition syndromes, and the results set forth herein should not be used as a substitute for tests validated to determine genetic risk.

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, particularly in the event that deleterious mutations are reported. The ordering physician or the patient is responsible for contacting a genetic counselor to discuss test results.

Tempus Insights

If this report includes a section titled "Tempus Insights", then in addition to the limitations above in this Disclaimer, the "Tempus Insights" are also subject to certain additional limitations, as described below.

Tempus may, in its sole discretion, populate patient reports with informational "Tempus Insights." Tempus Insights are observations that may be relevant to a specific patient based upon the similarity of the patient's clinical or molecular attributes with a subset of patients whose clinical and/or molecular data has been included in an internal Tempus database. Where appropriate (and/or available), the Tempus Insights have been presented with material information (e.g., supporting PubMed citation, size of the population underlying the Insight) and/or statistical analyses (e.g., p-values, confidence intervals) intended to give the ordering physician adequate context to evaluate the potential relevance of the Insight to the patient.

Tempus derives the "Tempus Insights" from the analysis of Tempus' own internal dataset. The data that populate this dataset are, in many cases, gathered from real-world settings (as opposed to within controlled clinical trials), and as such, the analyses run thereon may be subject to certain biases that restrict their generalizability or applicability to individual patients. The data that comprise the Tempus dataset may not be representative of patient populations as a whole, nor relevant to this patient specifically.

The Tempus Insights are current as of the date provided, and reflect the analysis of the patient's specific data and the internal Tempus database as of the date thereof. Tempus' dataset grows over time and, as a result, the Insight(s) generated from the analysis of the Tempus dataset may (or may not) change as the Tempus dataset includes additional data. Tempus will not update the Tempus Insights, even insofar as subsequent changes to the Tempus dataset would have led to additional and/or contradictory Insights if the Tempus database were to be re-queried with the patient's information.

Tempus provides the "Tempus Insights" for informational purposes only, and strongly encourages the patient's physician to consider all available information and options for obtaining additional information before making any patient-specific management or treatment decisions. All context should be taken into account when making a decision for any patient, and in no case should the Tempus Insights be cited as sufficient evidence in any clinical decision.

Any language specific to the insight(s) generated for the patient will be noted below.

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.

Diagnosis
Solitary fibrous tumor

Accession No.

IHC

Date of Birth
01/01/1954

Sex
Male

Physician
Raphael Borok

Institution
Precision Diagnostic Laboratory 1966427

TEMPUS | IHC

Analysis performed using DAKO PD-L1 22C3 clone.

Tumor specimen:
Mediastinum

[redacted]

PD-L1 EXPRESSION

Negative

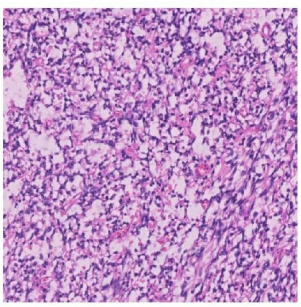
Tumor cell staining (membranous)

<1%

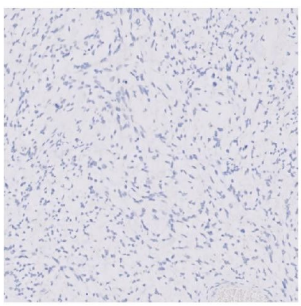
Tumor-associated immune cell staining

<1%

200x



H&E



PD-L1

Interpretation Guidelines

PD-L1 positive staining is defined as complete circumferential and/or partial linear plasma membrane staining of tumor cells at any intensity. PD-L1 IHC 22C3 pharmDx is a qualitative immunohistochemical assay using Monoclonal Mouse Anti-PD-L1, Clone 22C3 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) non-small cell lung cancer (NSCLC), gastric or gastroesophageal junction (GEJ) adenocarcinoma, cervical cancer and urothelial carcinoma tissues. See the KEYTRUDA® product label for expression cutoff values guiding therapy in specific clinical circumstances.

[redacted]

Tempus Disclaimer (continued)

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.