The Tempus Report

At Tempus we offer a report for each patient that highlights key findings, including potentially actionable alterations, immunotherapy markers and clinical trial options that can help inform patient care.

GENOMIC VARIANTS

Clinically relevant somatic alterations, incidental germline findings, and pertinent negatives.¹

Somatic Classification

Potentially Actionable 🕞 BRCA2

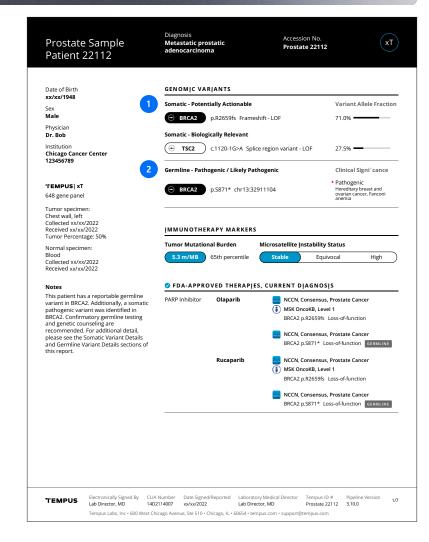
A somatic alteration that has a functional significance or association with the disease state and has associated therapeutic, prognostic or diagnostic evidence.

Biologically Relevant 🕞 TSC2

A protein-altering somatic alteration that may have functional significance or may have been observed in the medical literature but is not associated with a specific therapy in the Tempus knowledge database.

Germline Classification²

Pathogenic and likely pathogenic incidental germline variants are reported when a normal sample is provided. These are variants that are associated with inherited cancer syndromes, based on ACMG recommendations, NCCN guidelines and other published literature.



- 1 Select cancer types display disease associated genes for which no alterations were identified in the specimen that was tested.
- 2 Tempus xT is not a validated germline panel. The incidental germline findings are reported in a limited set of genes when sequencing a normal match specimen. Confirmatory germline testing with an appropriate test may be recommended for further evaluation, if clinically indicated.
- **3** Certain states require a signed patient consent to release germline results.

IMMUNOTHERAPY MARKERS

Key decision drivers for immunotherapy identified by our proprietary sequencing technologies and molecular profiling.

Tumor Mutational Burden (TMB)

A measurement of the quantity of mutations carried by a tumor. TMB is calculated as the number of all proteinaltering (non-synonymous) mutations per million base pairs of DNA covered by the Tempus panel. A TMB of ≥ 10 m/Mb is designated as TMB-high.

Microsatellite Instability (MSI)

A reference for the amount of genomic instability that results from impaired DNA mismatch repair (MMR) activity. A high level of microsatellite instability is noted as MSI-High.

Immunohistochemistry (IHC)

Tempus offers four (4) different PD-L1 IHC clones to assess PD-L1 expression, as well as a DNA mismatch repair (MMR) IHC panel.

FDA-APPROVED THERAPIES

FDA-approved therapies organized by level of evidence with associated NCCN xccx and MSK OncoKB (1) tags, highlighting response or resistance evidence.

Tempus also designates previously prescribed therapies in gray italic font, based on the clinical documents received (smart therapies).

CLINICAL TRIALS

A select list of clinical trials matched to genomic features, cancer type, clinical history, and distance from the patient's point-of-care.

LOW COVERAGE REGIONS

Low Coverage Regions are included when mean coverage over any region(s) of a gene falls below a threshold of 35x in the tumor sample. The absence of alterations in genes with low coverage should be interpreted carefully in the context of the patient's diagnosis with consideration for retesting.

VARIANTS OF UNKNOWN SIGNIFICANCE

DNA alterations identified with weak or ambiguous evidence of relevance to cancer biology.

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Received xx/xx/202 Tumor Percentage:		ÍMMUNOTHE	RAPY MARKER	5		
Normal specimen:		Tumor Mutatio	nal Burden	Microsatellite	Įnstability Status	
Blood Collected xx/xx/202	17	5.3 m/MB				
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	Talazoparib	NCCN, Consensus, Breast Cancer BRCA2 p.R2659fs Loss-of-function BRCA2 p.S871* Loss-of-function GERMLINE
Combination (PARP Inhibitor Olaparib + Bevacizumab + Anti-VEGF MAb)		NCCN, Consensus, Ovarian Cancer BRCA2 p.R2659fs Loss-of-function BRCA2 p.S871* Loss-of-function GERMLINE
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CLĮNĮCAL TRĮ	ALS	
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	rial of Nab-sirolimus in Patients With Ma ations in TSC1 or TSC2 Genes (PRECISIO)	
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SOMATIC AND GERMLINE VARIANT DETAILS

Additional clinical context for reported somatic and germline variants that are classified as pathogenic or likely pathogenic.

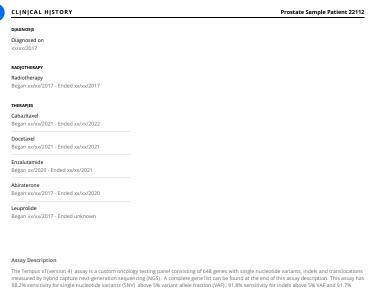
Variant allele fraction c.2459A>G p.K820R Missense variant NM_016578 PIK3C2B c.1034+5G>T Splice region variant NM 002646 PRKDC c.2900C>G p.P967R Missense variant NM 006904 19.4% c.185T>C p.M62T Missense variant NM 133331 18.6% BCR c.3457+4A>T Splice region variant NM 004327 c.1391T>G p.V464G Missense variant NM 007218 c.1108G>C p.E370Q Missense variant NM_004343 15.5% SOMATĮC VARĮANT DETAĮLS - POTENTĮALLY ACTĮONABLE → BRCA2 c.7975del p.R2659fs NM_000059 Frameshift - LOF BRCA2 encodes a nuclear phosphoprotein which helps maintain DNA stability through homologous recombination based DNA double stranded break repair and involvement in DNA damage checkpoint control. Loss of function mutations and copy number loss of BRCA2 are associated with cancer progression. SOMATIC VARIANT DETAILS - BIOLOGICALLY RELEVANT ⊕ TSC2 c.1120-1G>A NM_000548 Splice region variant - LOF VAF: 27.5% TSC2 encodes a protein, tuberin, that interacts with the protein encoded by TSC1, hamartin. These proteins are involved in the regulation of the PISK-AKT-mTOR pathway, a pathway involved in cell proliferation and survival. Loss of function mutations and copy number loss of TSC2 are associated with cancer progression. GERMLĮNE VARĮANT DETAĮLS ● BRCA2 c.2612C>A p.S871* NM_000059 chr13:32911104 Stop gain BRCA2 encodes a nuclear phosphoprotein which helps maintain DNA stability through homologous recombination based DNA double stranded break repair and involvement in DNA damage checkpoint control. Germline pathogenic variants in BRCA2 have been associated with autosomal dominant hereditary breast and ovarian cancer syndrome, which results in an increased risk of breast, ovarian, and fallopian tube cancers in women. Men with pathogenic variants in BRCA2 are at an increased risk to develop breast and prostate cancer, and both men and women are at an increased risk to develop pancreatic cancer (PMID: 33406487). Additionally, BRCA2 is associated with the autosomal recessive condition Fanconi anemia, heterozygotes are considered carriers, while homozygotes or compound heterozygotes are likely to be affected (PMID: 15070707). Clinical correlation, including confirmation of this variant through a validated germline assay, and genetic counseling are recommended for this patient and any potentially at-risk family members.

Prostate Sample Patient 22112

VARIANTS OF UNKNOWN SIGNIFICANCE (CONTINUED)

8 CLINICAL HISTORY

A timeline of the patient's clinical history including past procedures and treatments, informing reported smart therapy implications.



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Vers 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. Biologically Relevant alterations are protein-altering variants exhibiting an unclear effect on function and/or without sufficient evidence to determine their pathogenicity, Benign variants are not reported. Low Coverage Regions are included when mean coverage over any regions of a gain english below at threshold six in the tumor sample. The absence of alterations in genes with low coverage should be interpreted carefully in the context of the patient's diagnosis with consideration for retesting. Variants are identified through aligning the patient's DNA sequence to the human genome reference sequence version ingli of (Richtar). The clinical summary (first page of the report) shows actionable and bloogically relevant somatic variants, and certain pathogenic or likely asthogenic 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 at the number of protein-latering mutations per million coding base pairs. TMB is calculated at the time of initial report delivery. Accordingly, the TM calculation is based upon (a) both the tumor and normal sample if rempus had analyzed both 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 liked of response to

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Report Glossary

Genomic Variants

Mutations (+)

A change in the DNA sequence of a gene, which can be a somatic (acquired) or a germline (inherited) event. For each somatic mutation, Tempus provides a Variant Allele Fraction (VAF), which is the proportion of sequencing reads from the sample that contain the mutation of interest.

Copy Number Variations (CNV) (=) (=)

A deviation from the normal number of copies of a gene, which is typically 2. They are reported either as a Copy Number Gain (amplification) or a Copy Number Loss (deletion).

A Copy Number Gain is reported when ≥ 8 copies are detected, and a Copy Number Loss is reported when 2 copies are lost.

Loss of Heterozygosity (LOH)

Loss of Heterozygosity (LOH) occurs when there is loss of the second, wild-type copy of a gene that already has an inactivating alteration in the first copy. When LOH is detected for germline BRCA1 and BRCA2 variants, it is displayed as a copy number loss on the report, and the gene description for the copy number loss will note that somatic LOH was identified.

Chromosomal Rearrangements (Translocations) (1)

A change to the structure of a chromosome, such as a deletion, duplication, inversion or translocation. Chromosomal rearrangements can bring two distant gene fragments together to form fusion genes. This may result in expression of a fusion protein with new or enhanced function that contributes to tumorigenesis.

Tempus detects rearrangements (translocations) through two lines of sequencing: DNA sequencing for a subset of genes, and unbiased fusion transcript detection using whole transcriptome RNA sequencing.

Variant Details

Missense Variant

A genetic alteration in which a single base pair substitution alters the genetic code in a way that produces a different amino acid from the usual amino acid at that position in the protein. Some missense variants will alter the function of the protein.

Frameshift

Small insertion or deletion of a DNA sequence in the coding region of a gene that changes the reading frame of the protein and disrupts subsequent amino acid sequence. Typically results in a non-functional protein.

Stop Gain

DNA sequence change that causes a premature stop in the amino acid sequence of the protein. Typically results in a truncated, non-functional protein.

Splice Region Variant

DNA sequence change that results in exons of the gene being incorrectly spliced (or pasted) together, often with the result that an exon is excluded.

Gain-of-Function (GOF)

A DNA sequence change that results in a protein which has either increased or novel function

Loss-of-Function (LOF)

A DNA sequence change that results in a protein which loses normal function.

c.; p.

Designates a variant's effect at the nucleotide/mRNA level; at the amino acid/protein level.

NM_#

The RefSeg transcript number for the c. alteration.

Learn more

tempus.com/oncology/ →