Incredible Hulk

Diagnosis
Lung adenocarcinoma

Accession No.
TL-22-5NDUXKUG

HRD

Date of Birth
01/01/1990

Sex
Male

Physician
Test Physician

Institution
Test Insitution 123456789

TEMPUS | HRD

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

Normal specimen:
Collected 02/06/2022
Received 02/11/2022

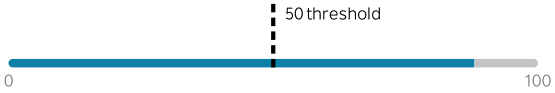
HOMOLOGOUS RECOMBINATION DEFICIENCY STATUS

Positive

HRD status is determined by a test that uses mRNA expression from the Tempus|xT assay to predict the probability that a tumor's gene expression profile correlates with well-characterized benchmarks of the HRD phenotype.

HRD Score

88



GENOMIC VARIANTS

To review additional details about the variants listed below, and sequencing results for genes outside of the Homologous Recombination Repair (HRR) pathway, please refer to the associated Tempus|xT report TL-22-F9RBJ7N7.

Genomic Variants - Pathogenic/Likely Pathogenic		Details
BRCA2	c.2808_2811del | p.A938fs Frameshift chr13:32911297 NM_000059	Germline

Genomic Variants of Unknown Signficance		Details
BRCA2	c.2808_2840delinsGCA | p.A938_L947del Inframe deletion NM_000059	31.9% VAF
CDK12	c.1610C>T | p.P537L Missense variant NM_016507	22.6% VAF

Assay Interpretation

Homologous Recombination Deficiency (HRD) is the phenotype characterized by the inability to repair DNA breaks via the homologous recombination repair (HRR) pathway. HRD is frequently driven by loss-of-function alterations in genes that compose the HRR pathway, the most well-characterized of which are BRCA1 and BRCA2.

The Tempus HRD test utilizes one of two separate versions of HRD determination. For breast and ovarian cancer patients (cancer type determined by Tempus pathology review), the determination method is DNA-based. For all other primary cancer types, the determination method is RNA-based.

For the DNA version, a positive Tempus HRD result is defined as biallelic loss-of-function alterations in BRCA1 or BRCA2, and/or genome-wide loss of heterozygosity (GWLOH) above a specified cancer type-dependent threshold. GWLOH is considered positive for HRD at ≥ 21% for breast cancer and ≥ 17% for ovarian cancer.

For the RNA version, HRD is assessed by evaluating RNA expression of 20,000 genes. Data generated from Tempus RNA sequencing is used to assess gene expression levels and calculate an RNA HRD score. A positive Tempus HRD test is defined by an RNA HRD score above a threshold of 50. Scores are designed to be interpreted as the probability that the tested sample is HRD-positive. Biallelic loss-of-function alterations in BRCA1/2 do not impact the RNA HRD result. For that reason, a specimen assessed as HRD-Not Detected based on RNA analysis may nonetheless exhibit bi-allelic BRCA1 and/or BRCA2 alterations.

BRCA1 and BRCA2 alterations considered positive for HRD using the DNA version include a pathogenic or likely pathogenic alteration with BRCA1/2 loss of heterozygosity (LOH), biallelic pathogenic or likely pathogenic alterations, and two copy loss. BRCA1/2 copy number status is computed using the Tempus copy number calling algorithm (CONA), which uses tumor purity and copy states in the tumor genome to generate copy number and loss-of-heterozygosity calls.

Assay Description

The Tempus HRD test utilizes one of two separate versions of HRD determination. For breast and ovarian cancer patients, the determination method is DNA-based. For all other primary cancer types, the determination method is RNA-based. The Tempus HRD DNA version uses results from tumor and normal matched xT sequencing to calculate the GWLOH percentage and the somatic and germline alteration status of BRCA1 and BRCA2 to determine HRD status. GWLOH is determined by the length-weighted percentage of probed regions with LOH by the Tempus copy number calling algorithm (CONA).

The RNA version uses results from tumor RNA sequencing to determine RNA expression levels and calculate an RNA HRD score, and uses that score to determine HRD status. RNA HRD score is calculated by processing gene expression values through a logistic regression model trained to predict bi-allelic BRCA loss.

HR-pathway genes analyzed on the Tempus|xT panel include ATM*, ATR, ATRX, BAP1, BARD1, BLM, BRCA1*, BRCA2*, BRIP1*, CDK12, CHEK1, CHEK2*, FANCA, FANCL, HDAC2, MRE11, NBN*, PALB2*, RAD50, RAD51B, RAD51C*, RAD51D*, RAD54L. Alterations in these genes will be identified on the Tempus HRD report. To review additional details about the variants listed for HR-pathway genes, and sequencing results for genes outside of the HR pathway, please refer to the associated Tempus|xT report.

*Genes in which incidental germline findings are reported

Tempus Disclaimer

The Tempus HRD test uses information from analysis of nucleic acids by next-generation sequencing (NGS). That analysis, and the resulting information, can be affected by multiple factors including formalin-fixation degrading DNA or RNA quality, and low tumor purity limiting sensitivity of the assay. Additionally, the chance of detecting genetic and transcriptomic alterations from NGS may be reduced in regions of the genome that are structurally difficult to sequence, in homologous genes, or due to sequencing artifacts or errors. The Tempus HRD test is reported only for cases with greater than or equal to 30% tumor purity for the RNA version and 40% tumor purity for the DNA version.

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 or changes to HRD status based on new information or alternate methods of determining HRD status. No guarantee can be made that determination of an HRD phenotype indicates whether a patient will respond to any treatment or therapy.

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.