HRD Testing

Homologous Recombination Deficiency (HRD) is defined as the inability of the cell to repair DNA via the Homologous Recombination Repair (HRR) pathway. HRD is frequently driven by loss of function alterations in the BRCA1/2 gene in addition to other HRR pathways genes, and is associated with genomic loss of heterozygosity (LOH). Tempus HRD is a DNA-based laboratory developed test, available as an additional test for patients who receive Tempus|xT Solid Tumor + Normal Test. The HRD test is used to identify patients who may be sensitive to PARP inhibitors and/or platinum-based chemotherapy[1-5].

HRD Test Advantages

No Additional Tissue Required

The Tempus HRD test conserves tissue by using data derived from xT Solid Tumor + Normal test. The HRD test can be ordered alongside xT without the need for additional tissue. In addition to utilizing HRD testing in cancer subtypes with relatively high frequency of HRD, this workflow facilitates HRD analysis in cancer types where HRR pathway alterations are rare, but where there may be suspicion of HRD based on DNA sequencing results.

Complete Patient View

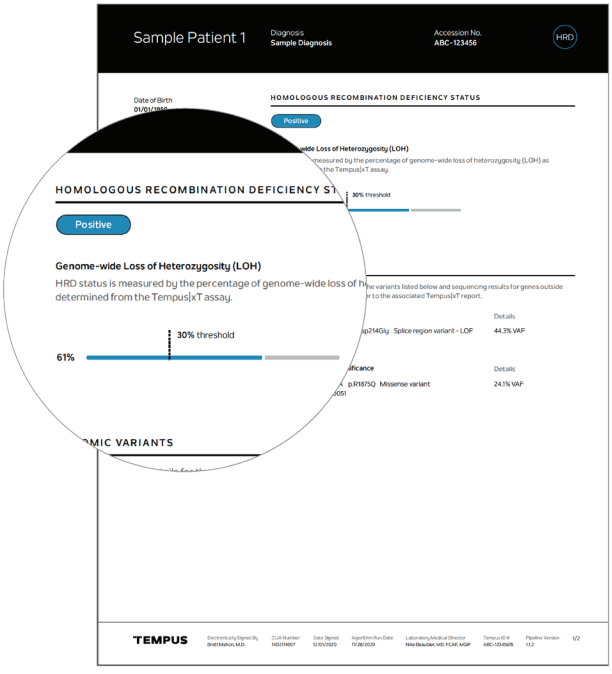
When ordered together, xT Solid Tumor + Normal Test and HRD results provide physicians with insight into somatic and germline alterations assessed through DNA sequencing, comprehensive and unbiased detection of gene fusion events through RNA sequencing, and HRD status. This multi-analyte testing approach provides physicians with an in-depth view into the genomic characteristics of their patients' tumor to facilitate their treatment decisions.

HRD Report Features

1. **Simple to use HRD Status**
   Report will show status as "Positive" or "Not Detected". The test returns an HRD "positive" result if there is evidence for biallelic inactivation of BRCA, or the genome-wide LOH estimate of the sample is greater than a cohort-specific threshold (LOH high).

2. **Genome-wide LOH Percentage**
   Genome-wide LOH score is calculated and shown in comparison to the tumor-specific threshold for HRD positivity. This threshold is 0.25 for Ovarian Cancer, 0.29 for Breast Cancer, 0.28 for Pancreatic Cancer, and 0.33 for all other cancer types[6].

3. **List of Homologous Recombination Repair Mutations (HRRm) from our xT Panel**
   The report additionally highlights genomic alterations detected by the xT Test in these 18 genes: ATM, BARD1, BRCA1, BRCA2, BRIP1, CDK12, CHEK1, CHEK2, FANCA, FANCL, HDAC2, MRE11, NBN, PALB2, RAD51B, RAD51C, RAD51D, RAD54L.



1. Gonzalez-Martin, et al. "Niraparib in Patients with Newly Diagnosed Advanced Ovarian Cancer". N Engl J Med 2019;381:2391-402
2. Swisher, et al. "Rucaparib in Relapsed, Platinum-Sensitive High-Grade Ovarian Carcinoma (ARIEL2 Part 1): An International, Multicentre, Open-Label, Phase 2 Trial". The Lancet Oncology, Volume 18, Issue 1, 75-87
3. Mirza, et al. "Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer". N Engl J Med 2016; 375:2154-2164
4. NCCN Guidelines Version 1.2020: Pancreatic Adenocarcinoma
5. NCCN Guidelines Version 1.2020: Ovarian Cancer
6. Data on file. Tempus Internal Validation Report May 22, 2020