PAN-TUMOR

Homologous Recombination Deficiency Signature (HRDsig) in Solid Tumors

FOUNDATION MEDICINE®

What is HRDsig?

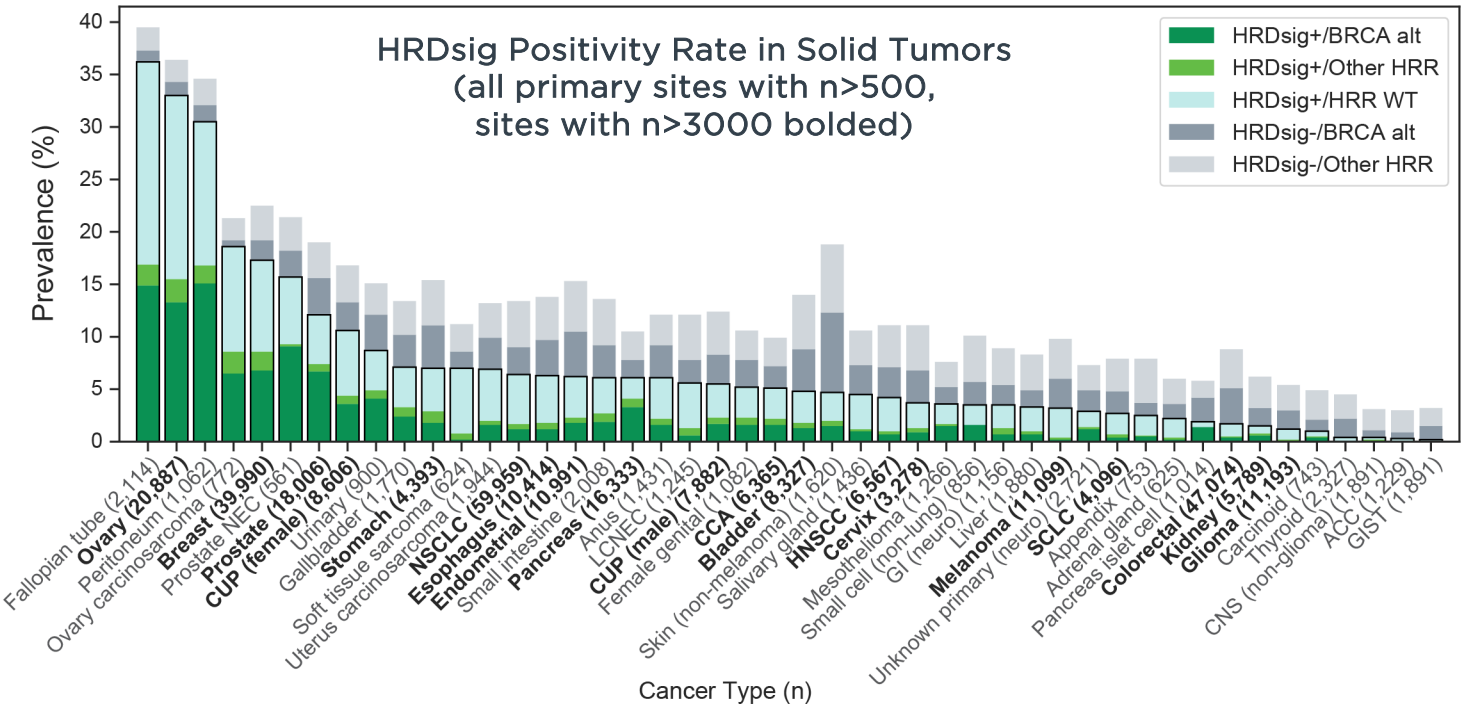
Homologous recombination deficiency (HRD) produces characteristic genome-wide changes that can be captured by analyzing segmented copy number (CN) profiles. **HRD signature (HRDsig) is a biomarker developed and validated to classify HRD status in pan-cancer samples using hundreds of CN features.**

This biomarker is reported on FoundationOne®CDx as a laboratory professional service that has not been reviewed or approved by the FDA; reporting categories are described below:

- Samples with score ≥0.7 are reported as **HRDsig Positive** and samples with score <0.7 are reported as **HRDsig Negative**. If the sample is not of sufficient quality to confidently determine CN features, the status is noted as **Cannot Be Determined**.
- The HRDsig score is not an HRD accumulation or probability score but rather a model score; it ranges from 0–1 and has a bimodal distribution, with most pan-cancer results falling between 0–0.2 or 0.8–1.
- *The score is provided as additional information but has not been validated as a stand-alone biomarker to support clinical decision making and should be integrated with other patient-specific factors, including cancer type and other genomic findings.*

HRDsig Positivity Rate by Tumor Type and HRR Status

- In the Foundation Medicine database, the pan-solid tumor frequency of HRDsig positivity is ~8%, with high frequencies observed in ovarian, prostate, and breast cancers.
- HRDsig positivity is seen in *BRCA*-altered, HRR gene-altered, and HRR wild-type tumors.



HRDsig Positivity by Tumor Type and BRCA Status

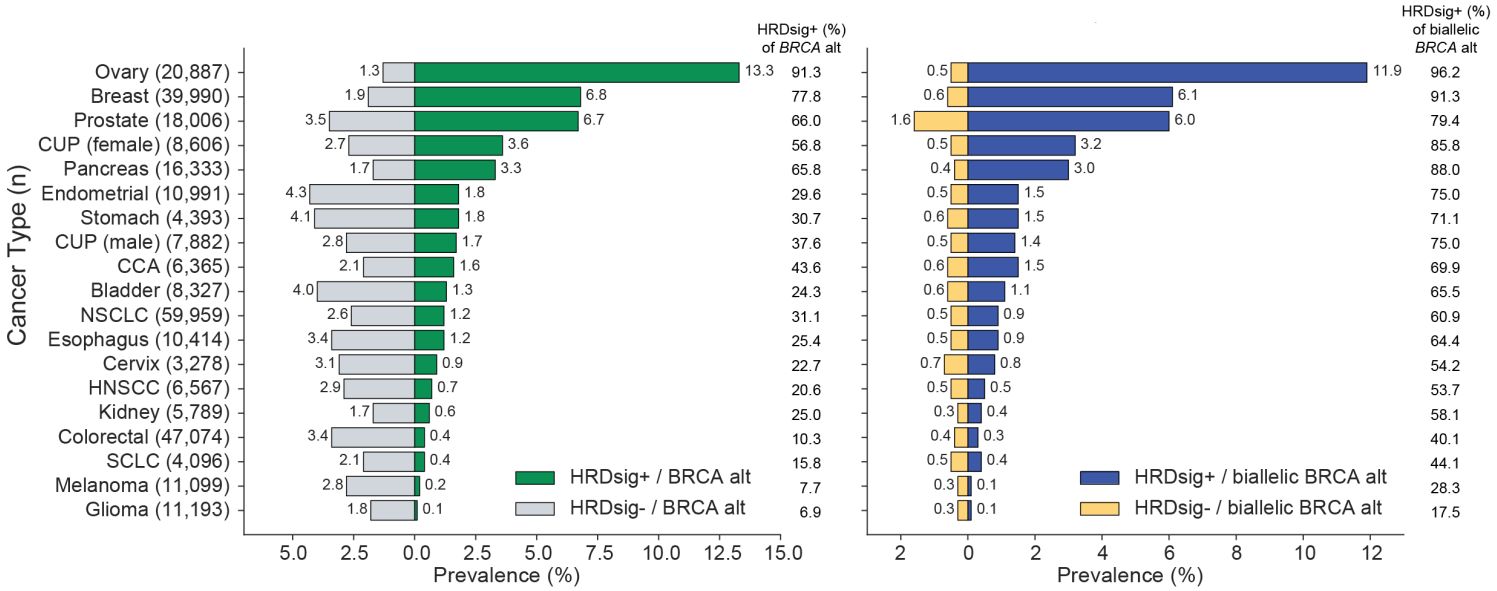
BRCA alterations and HRDsig positivity by tumor type (left panel)

- The proportion of *BRCA*-altered tumors with HRDsig positivity varies according to tumor type.
- In ovarian and breast cancers, a high percentage of *BRCA*-altered tumors display HRDsig positivity. However, in diseases like non-small cell lung cancer and colorectal cancer, only a small percentage of *BRCA* alterations are associated with HRDsig.

Biallelic BRCA alterations and HRDsig positivity by tumor type (right panel)

Across most solid tumor types, biallelic *BRCA* alteration is strongly associated with HRDsig positivity.

- The percentage of HRDsig positivity in biallelic *BRCA*-altered tumors is higher than in the overall *BRCA*-altered population.



Have questions about HRDsig? Contact Medical Affairs at med.info@foundationmedicine.com.

Abbreviations

ACC = adenoid cystic carcinoma, CCA = cholangiocarcinoma, CNS = central nervous system, CUP = cancer of unknown primary, GIST = gastrointestinal stromal tumor, HNSCC = head and neck squamous cell carcinoma, HRR = homologous recombination repair, HRDsig = homologous recombination deficiency signature, neuro = neurological, NSCLC = non-small cell lung cancer, SCLC = small cell lung cancer.

Reference

Data on File, Foundation Medicine, Inc., 2024.

HRDsig is reported as a laboratory professional service that has not been reviewed or approved by the FDA. FoundationOne®CDx is a qualitative next-generation sequencing based *in vitro* diagnostic test for advanced cancer patients with solid tumors and is for prescription use only. The test analyzes 324 genes as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) and is a companion diagnostic to identify patients who may benefit from treatment with specific therapies in accordance with the approved therapeutic product labeling. Additional genomic findings may be reported and are not prescriptive or conclusive for labeled use of any specific therapeutic product. Use of the test does not guarantee a patient will be matched to a treatment. A negative result does not rule out the presence of an alteration. Some patients may require a biopsy. For the complete label, including companion diagnostic indications and important risk information, please visit www.F1CDxLabel.com.