OVARIAN CANCER

Homologous Recombination Deficiency Signature (HRDsig) Clinical Data

FOUNDATION MEDICINE®

This document reviews clinical evidence for Foundation Medicine's HRDsig biomarker reported as a laboratory professional service on FoundationOne®CDx#. Key points include:

HRDsig positivity captures a genomically diverse HRD population with improved performance over gLOH

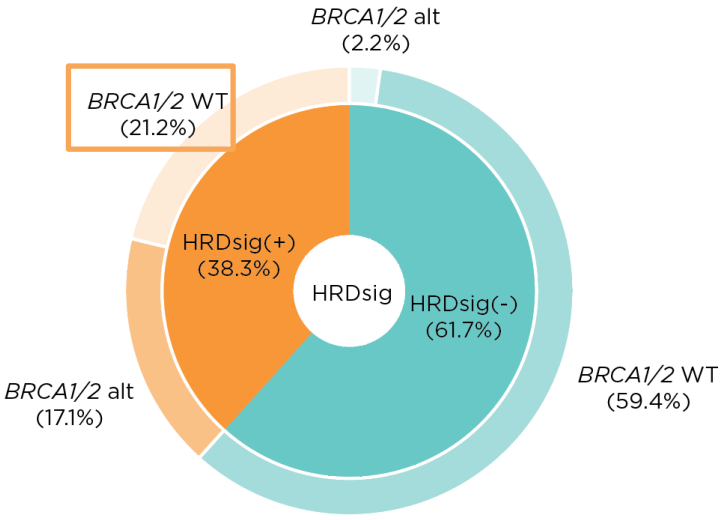
HRDsig detects an additional population compared to *BRCA1/2* genomic alterations alone

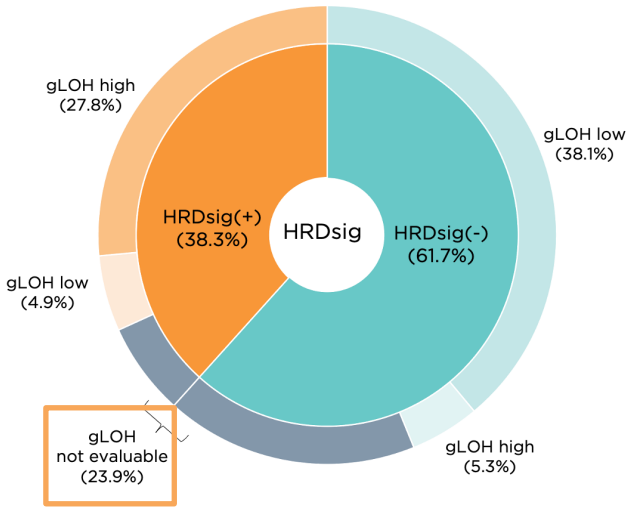
HRDsig Identifies Diverse Mechanisms of HRD

HRDsig-negative status is associated with *BRCA* wild-type status, while the HRDsig-positive population captures multiple mechanisms of HRD.[1,2]

In the Foundation Medicine database, the overall prevalence of HRDsig positivity in all subtypes of ovarian cancer is ~30-35%.[2] When limited to high grade serous ovarian cancer, the prevalence is ~50%.[1]

- HRDsig detects an additional population that may benefit from PARP inhibitors over *BRCA* genomic alteration alone.[2]
- HRDsig can be assessed for 24% of samples with genomic loss of heterozygosity (gLOH) not evaluable.[2]





In an analysis of the ARIEL2 trial population, HRDsig detected 98% of the *BRCA* methylation-positive population compared to 83% with gLOH, showing improved biomarker performance to detect non-genomic mechanisms of HRD.[3]

BRCA status	Percent HRDsig positive	Percent gLOH >16%
BRCA mutation	94%	86%
BRCA methylation	98%	83%
No *BRCA* mutation/methylation	48%	49%

#HRDsig is reported as a laboratory professional service that has not been reviewed or approved by the FDA.

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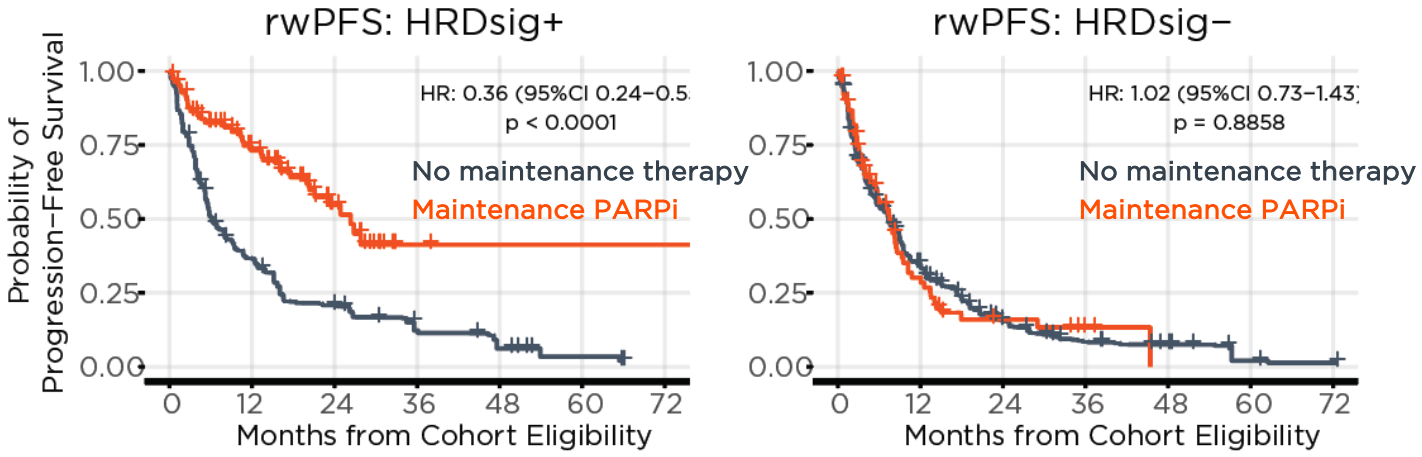
HRDsig Positivity Is Associated With Real-World PFS on Maintenance PARPi After Platinum Chemotherapy[2]

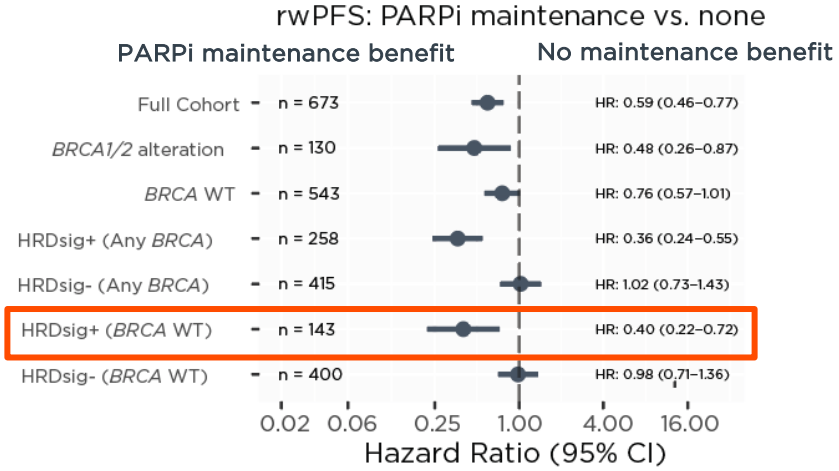
In an analysis of the Flatiron Health-Foundation Medicine Clinico-genomic Database, HRDsig-positive status was associated with longer median real-world progression-free survival (rwPFS) with the addition of a maintenance PARP inhibitor (PARPi).

This rwPFS benefit was not observed in the HRDsig-negative population.



HRDsig and Maintenance Therapy in BRCA Wild-Type Ovarian Cancer[2]

- In the *BRCA* wild-type (unmutated) subset of the cohort, HRDsig positivity was associated with longer rwPFS on maintenance PARPi.
- This rwPFS benefit was not observed in the *BRCA* wild-type, HRDsig-negative population.



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

References

1. Data on File, Foundation Medicine, Inc., 2024. 2. Richardson D, et al. *Clinical Cancer Res*. 2024 doi:10.1158/1078-0432.CCR-24-1225. 3. Sokol E, et al. Poster presented at AACR 2023. Abstract 966.

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.