FRIENDS of CANCER RESEARCH

HRD Harmonization Project

The Definition: Homologous recombination (HR) status is a complex biomarker that helps identify whether patients may respond to certain treatments. This biomarker has promise to identify patients with certain cancers who are more likely to benefit from PARP inhibitors or other DNA repair targeting drugs. Tumors that are **HR deficient (HRD)** have a higher likelihood of responding to these therapies compared to tumors that are HR proficient (HRP).

The Problem: Currently, there is no standardized way to define, measure, and report HR status. Assays to determine HR status use different approaches to define HRD. There is no agreement on which parameters should contribute to the determination of HR status, potentially resulting in variability of HR status determination and generalizability of emerging clinical trial data. This could impact uptake and use of this biomarker in clinical care.

The Solution: **Friends of Cancer Research (*Friends*)** established a unique research partnership to develop strategies for assessing assay performance and aligning methods for measuring HRD and its use as a biomarker in clinical care. *Friends* assembled a consortium of project partners from key healthcare sectors to address concerns about the lack of consistency in determining HR status, its prognostic value, and its use as a predictive biomarker.

The Research Question: What are best practices for HRD assay alignment and analytical validation?

Workflow	Phase 1 Discovery and Definition	Phase 2 Assay Alignment	Phase 3 Clinical Contextualization
Objectives	• To refine the way HRD is utilized • To better understand how HR status calls are determined • To propose common language around the use of HRD	• To understand the level of variability across HRD assays • To identify opportunities for harmonization • To propose best practices for HRD assay alignment and use	• To explore how disease context impacts association between HRD and clinical outcome • To identify approaches for the development of clinical evidence to evaluate HRD
Approach	Developed a landscape analysis of HRD aimed to identify how HRD is used, define how HRD calls are made, and propose common language around the use of HRD.	Working through an analysis plan including multiple diagnostics companies to identify variability in HRD assays and opportunities for harmonization.	Report findings from Phase 2 for clinicians and patients, and develop an analysis plan to evaluate impacts of HRD testing on clinical efficacy.

Why Is This Important? The HRD Harmonization Project will support an understanding of the variability among HRD assays and provide suggestions for improved alignment moving forward. With this understanding, providers and patients will be better equipped to make the best decisions for treatment and care.

Who Is Involved? *Friends* is proud to partner with AbbVie, ACT Genomics, Ambry Genetics, Amoy Diagnostics, AstraZeneca, Arizona State University, Bayer, Bionano Genomics, Inc., Bristol Myers Squibb, Caris Life Sciences, DNAnexus, EMD Serono, Inc., European Organisation for Research and Treatment of Cancer (EORTC), the U.S. Food and Drug Administration (FDA), Foundation Medicine, Inc., GlaxoSmithKline, Guardant Health, Inc., Illumina, Inc., Invitae, Janssen, MD Anderson Cancer Center, Merck & Co., Inc., Molecular Characterization Laboratory (MoCha) at Frederick National Laboratory, NCI, Myriad Genetics, the National Cancer Institute (NCI), NeoGenomics, Novartis, OmniSeq, Personalis, Personal Genome Diagnostics (PGDx), Pfizer, Inc., Resolution Bioscience, Inc., SOPHiA GENETICS, Tempus Labs, Inc., Thermo Fisher Scientific, University of Alabama at Birmingham, University of Heidelberg