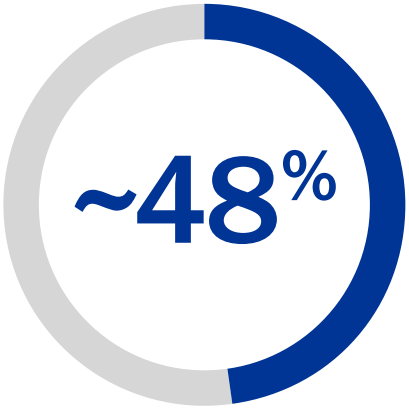
MyChoice® CDx

Myriad HRD Companion Diagnostic Test

Informing both early-line and late-line treatment decisions for patients with ovarian cancer

Myriad genetics

Health. Illuminated.



Homologous recombination deficiency (HRD) is present in approximately 48%[1] of ovarian cancer tumors, most often resulting from a mutation found only within the tumor.

Determining HRD status for ovarian cancer patients can help provide information on the magnitude of benefit for PARP inhibitor therapy.

Some causes of HRD are well established while others remain unknown[2-4]

1 in 2 patients with ovarian cancer are HRD+

1 in 4 HRD+ patients have a *BRCA1/2* mutation

- **25% have a tumor *BRCA1/2* mutation**
- 25% are other causes of HRD

Of ovarian cancer patients who are HRD+...

- **15%** Somatic
- **10%** Germline

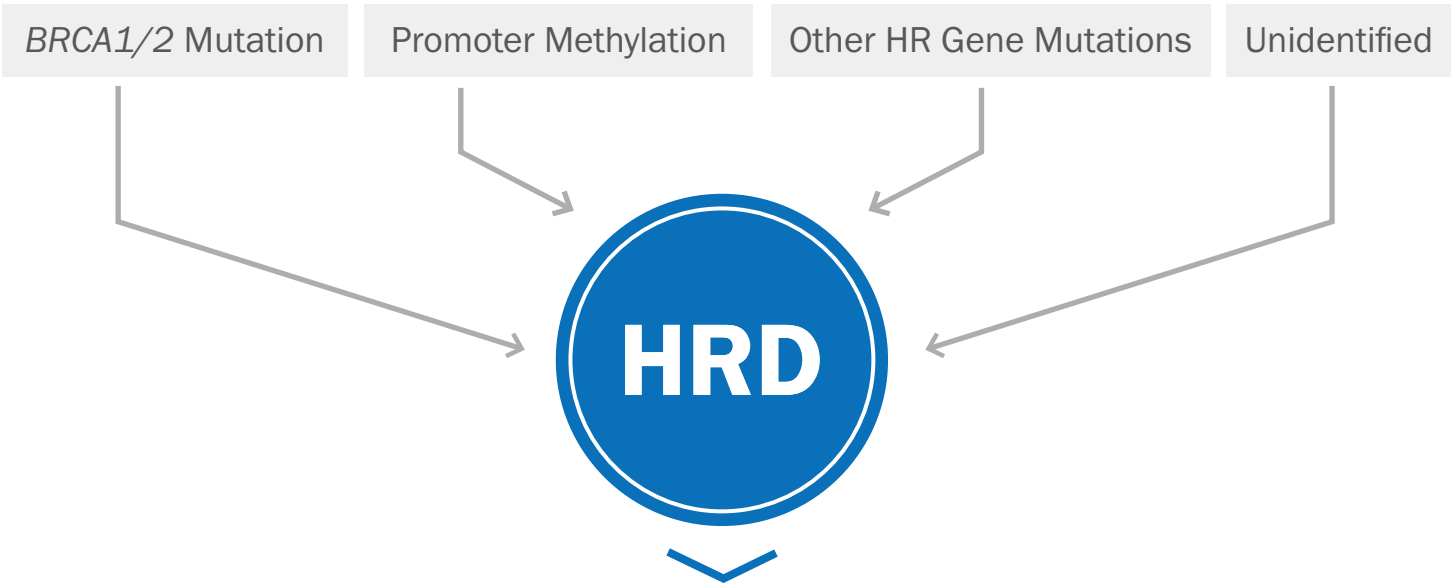
1. Moore et. al, Lancet Oncol 2019
2. Bonadio et al. Clinics 2018
3. Watkins et al. Breast Ca Res 2014
4. Panagiotis et al. Cancer Discov 2015
5. https://info.foundationmedicine.com/hubfs/FMI Labels/FoundationOne_CDx_Label_Technical_inifo.pdf.

There are limitations to determining HRD status when evaluating each cause individually

HRD resulting from epigenetic events such as *BRCA1* promoter methylation will be missed with a gene sequencing only approach[1,2]

HR pathway gene mutations other than *BRCA1* and *BRCA2* are rare and it is unclear if they are connected to HRD[3,4]

There is a distinct genomic effect associated with HRD[5]



LOH
Loss of Heterozygosity

TAI
Telomeric Allelic Imbalance

LST
Large-Scale State Transitions

Evaluating **LOH**, **TAI** and **LST** allows for the assessment of HRD regardless of the specific cause[5]

1. Timms et al. Br Ca Res 2014
2. Baldwin et al. Cancer Research 2000
3. Norquist et al. JAMA Oncol. 2016
4. The Cancer Genome Atlas. Nature 2011
5. Watkins et al. Breast Ca Res 2014

There are many ways HRD status can be measured

MyChoice® CDx examines ovarian cancer tumors using two individual methods (*BRCA1/2* mutation and genomic instability) to determine a patient's HRD status.

1 ***BRCA1* & *BRCA2* status** | **Sequence variants** + **Large rearrangements**

- Detection and classification of sequence variants and large rearrangements
- Identification of somatic and germline variants present in the tumor

2 **Genomic instability status** | **LOH** Loss of heterozygosity + **TAI** Telomeric allelic imbalance + **LST** Large-scale state transitions

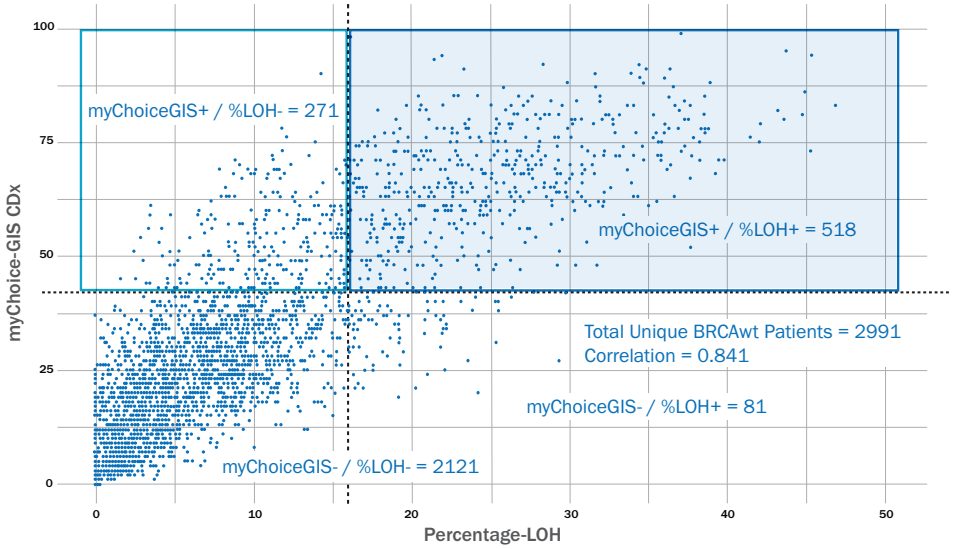
- Comprehensive assessment of LOH, TAI and LST across the entire genome

The MyChoice CDx approach

Uses 54,000 SNPs, capturing a more defined look into the genome vs %LOH which uses 3,500 SNPs only looking at a percentage of the genome.

Uses a platform technology that analyzes *BRCA1/2*, to include sequence variants and large rearrangements, capturing more than other platforms who do not have this technology.[2,3]

%LOH misses 34% of BRCA wild type samples that were identified as HR deficient by MyChoice® CDx[4]



1. Moore et. al, Lancet Oncol 2019
2. https://info.foundationmedicine.com/hubfs/FMI Lbels/FoundationOne_CDx_Label_Technical_Info.pdf
3. Timms, et al. JClinOnc 2020 38:15_suppl, 1586-1586.
4. Mills et al. Presentation for 2020 SGO Annual Meeting. SGO Annual Meeting on Women's Cancer (Abstract 1).

MyChoice® CDx

Myriad HRD Companion Diagnostic Test

MyChoice® CDx can inform early-line treatment decisions with LYNPARZA® (olaparib) and late-line treatment decisions with ZEJULA® (niraparib)

MyChoice® CDx intended use

Myriad MyChoice® CDx is a next generation sequencing-based *in vitro* diagnostic test that assesses the qualitative detection and classification of single nucleotide variants, insertions and deletions, and large rearrangement variants in protein coding regions and intron/exon boundaries of the *BRCA1* and *BRCA2* genes and the determination of Genomic Instability Score (GIS) which is an algorithmic measurement of Loss of Heterozygosity (LOH), Telomeric Allelic Imbalance (TAI), and Large-scale State Transitions (LST) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens.

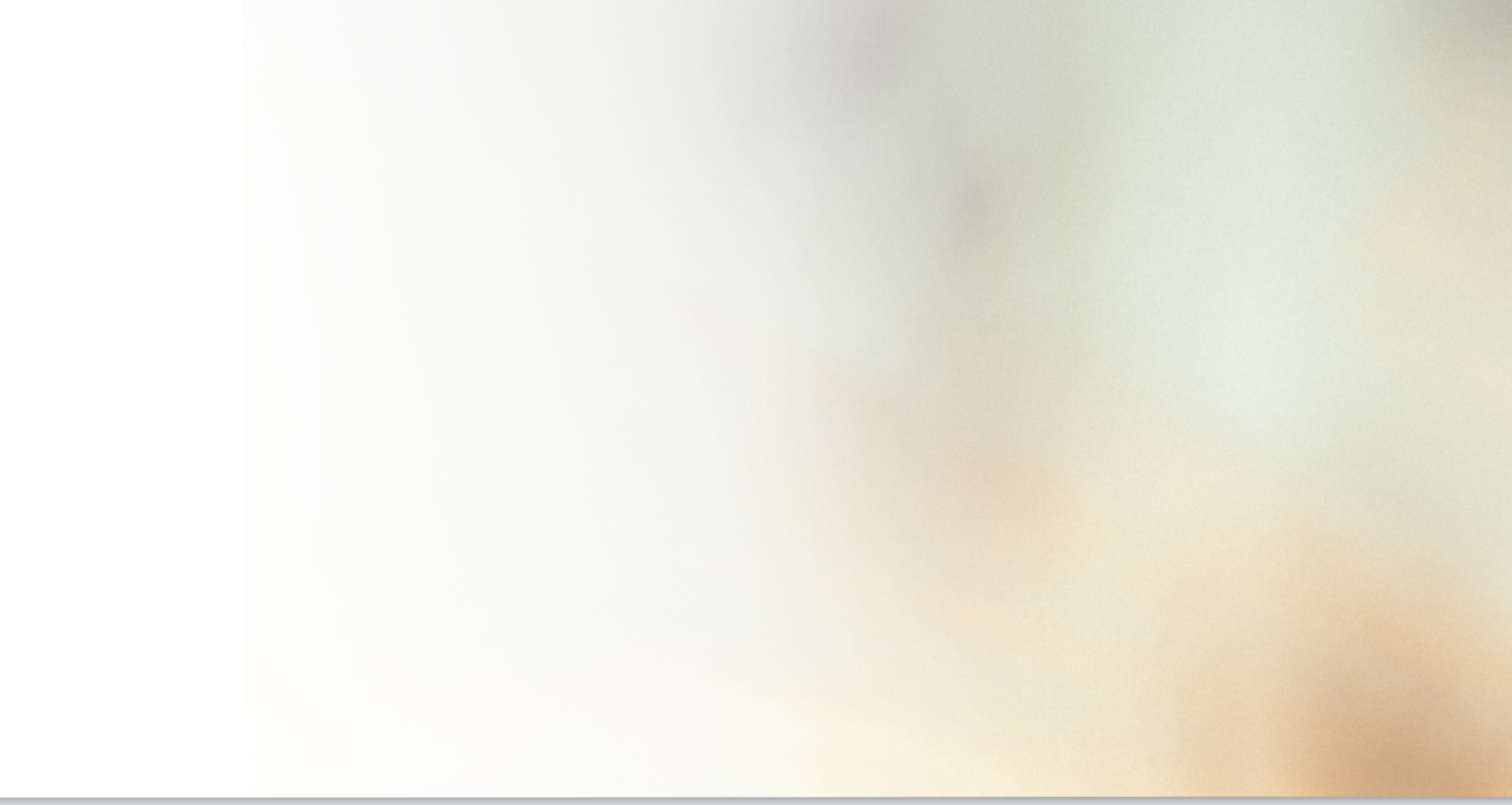
The results of the test are used as an aid in identifying ovarian cancer patients with positive homologous recombination deficiency (HRD) status, who are eligible, because of a positive test result for deleterious or suspected deleterious mutations in *BRCA1* or *BRCA2* genes, or may become eligible, because of a positive test result for deleterious or suspected deleterious mutations in *BRCA1* or *BRCA2* genes or a positive Genomic Instability Score, for treatment with the targeted therapy listed in Table 1 in accordance with the approved therapeutic product labeling.

Table 1: Companion diagnostic indications

Tumor Type	Biomarker	Therapy
Ovarian Cancer	Myriad HRD, defined as: • deleterious or suspected deleterious mutations in *BRCA1* and *BRCA2* genes and/or • positive Genomic Instability Score	LYNPARZA® (olaparib)

*Refer to the drug label for HRD definition for olaparib monotherapy or combination therapy.

Detection of deleterious or suspected deleterious *BRCA1* and *BRCA2* mutations and/or positive Genomic Instability Score in ovarian cancer patients is also associated with enhanced progression-free survival (PFS) from ZEJULA® (niraparib) maintenance therapy, in accordance with the most recently approved therapeutic product labeling. This assay is for professional use only and is to be performed only at Myriad Genetic Laboratories, Inc., a single laboratory site located at 320 Wakara Way, Salt Lake City, UT 84108.



Not all HRD tests are alike

	Myriad MyChoice® CDx	Caris Molecular Intelligence	Foundation Medicine FoundationOneCDx	Tempus Tempus xT
Landmark published clinical trials	**Quadra, Paola, Prima, SOLO**	None	SOLO, Ariel	None
Guidelines	**ASCO (by name), NCCN**	None	ASCO (For BRCA)	None
FDA-approval	**Yes***	No	Yes	No
HRD markers	**tBRAC, LOH, TAI, LST**	tBRAC, %LOH	tBRAC, %LOH	tBRAC
Comprehensive *BRCA1/2* large rearrangements performed?	**Yes**	No	No	No

* MyChoice CDx received FDA-approval in October 2019 with broad insurance coverage

1. Mills, G. et al. Presentation for 2020 SGO Annual Meeting. SGO Annual Meeting on Women's Cancer (Abstract 1).
2. Moore, K. et al. (2018). Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer. N Engl J Med. Published. https://doi.org/10.1056/NEJMoa1810858Moore, K. et al. (2019). Niraparib monotherapy for late-line treatment of ovarian cancer (QUADRA): a multicentre, open-label, single-arm, phase 2 trial. Lancet. Published. https://doi.org/10.1016/S1470-2045(19)30029-4
3. Ray-Coquard, I. et al. (2019). Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. N Engl J Med. Published. https://doi.org/10.1056/NEJMoa1911361
4. Gonzalez-Martin, A. et al. (2019). Niraparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med. Published. https://doi.org/10.1056/NEJMoa1910962

ASCO exclusively cites the MyChoice® CDx Test for patients with advanced ovarian cancer

The American Society of Clinical Oncology (ASCO) has exclusively included Myriad's MyChoice® CDx test in its new recommendations on the use of PARP inhibitors for the treatment and management of certain patients with advanced ovarian cancer. The new recommendations, based on clinical trial results, were published in September 2020 in the Journal of Clinical Oncology.

ASCO's guideline provides a scenario-based set of recommendations as to when PARPi therapy may and should be offered. The guideline specifically names MyChoice CDx in the "recommendations" section and is the **only** commercial companion diagnostic with such a designation. The guideline also includes MyChoice CDx guided management in both newly diagnosed and recurrent ovarian cancer.

Read the full article: https://ascopubs.org/doi/full/10.1200/JCO.20.01924?af=R

MyChoice® CDx delivers affordable results in 14 days or less*

MyChoice CDx order process

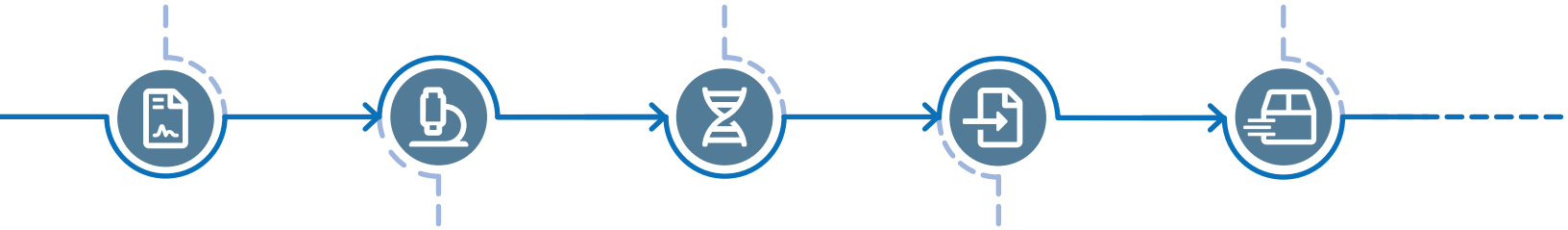
Provider completes the test request form (on the portal or paper TRF)

Myriad Genetics receives the TRF and sends a tumor specimen collection kit to the pathology lab

Tumor sample** arrives at Myriad Genetics lab and MyChoice CDx testing is performed*

Results are sent to the ordering provider (on the portal or in the mail)^

Tumor block is returned to the pathology lab immediately after result reporting
(slides will not be returned)



*Upon receipt of tumor specimen
**MyChoice CDx is run on formalin-fixed paraffin-embedded (FFPE) ovarian tumor tissue
^ Results may be sent to the pathologist on the portal or in the mail

If you have questions about the test or ordering process, Myriad experts are available to assist you:

Customer Service: **mychoicecdx@myriad.com | 877-283-6709**

Clinical Support: **helpmed@myriad.com**

Myriad genetics

Myriad Genetics, Inc. 320 Wakara Way, Salt Lake City, UT

www.myriad-oncology.com/mychoice-cdx