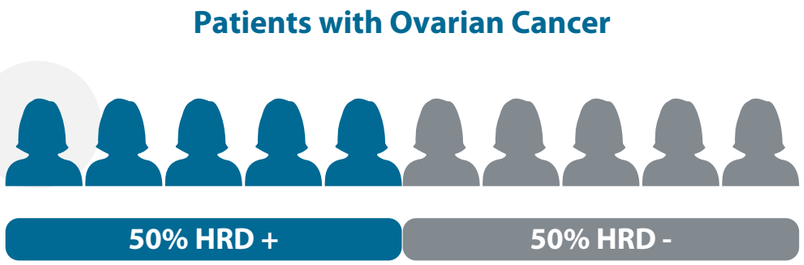
MYRIAD myChoice® CDx PLUS

The most comprehensive HRD tumor test to guide PARP inhibitor treatment decisions

myriad®
WHEN DECISIONS MATTER

Not for distribution in the US.

Homologous recombination deficiency (HRD) is present in approximately 50%[1,2] of ovarian cancer tumors

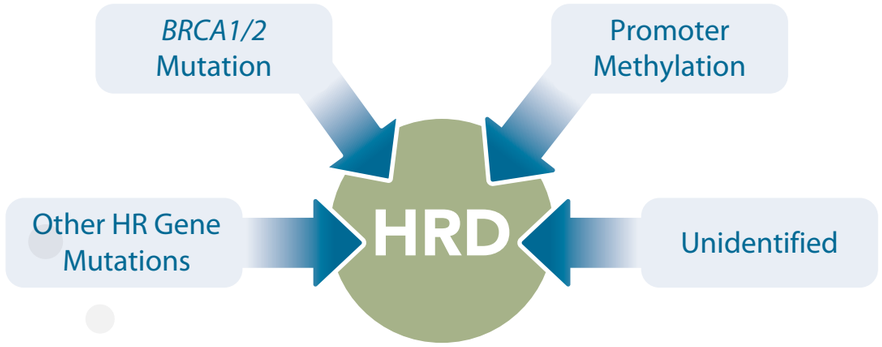


There are limitations to determining HRD status when evaluating each cause individually

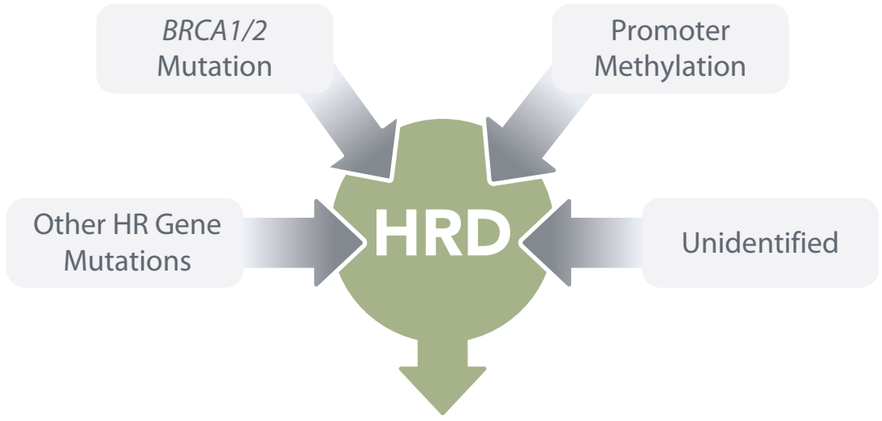
HRD resulting from epigenetic events such as ***BRCA1*** promoter methylation will be missed with a gene sequencing approach[1,2]

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

Some **CAUSES** of HRD are well established while others remain unknown[3,4,5]



There is a distinct genomic **EFFECT** associated with HRD[5]



Evaluating **LOH, TAI** and **LST** allows for the assessment of HRD regardless of the specific cause[3]

1. The Cancer Genome Atlas. Nature 2011
2. Yates et al. Annals of Oncology 2014
3. Bonadio et al. Clinics 2018
4. Watkins et al. Breast Ca Res 2014
5. Panagiotis et al. Cancer Discov 2015

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

myChoice® CDx PLUS is a tumor test that determines HRD status by measuring *BRCA1* and *BRCA2* mutation status and Genomic Instability Status through proprietary methods

1 *BRCA1 & BRCA2* Status | **Sequence Variants** + **Large Rearrangements**

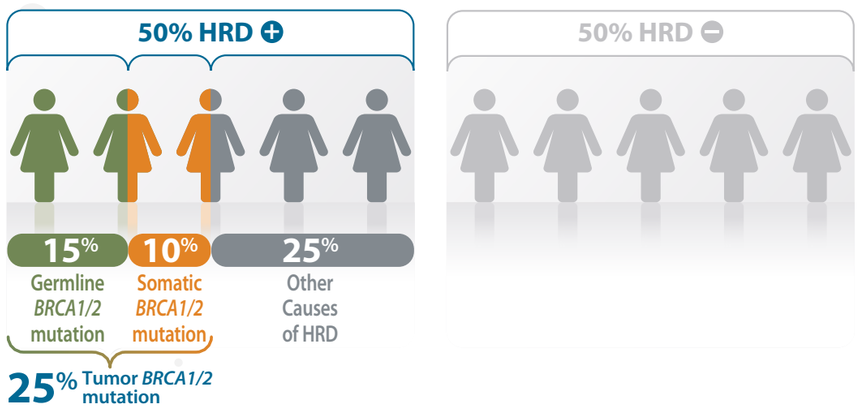
- Detection and classification of sequence variants and large rearrangements
- Identification of somatic and germline variants present in the tumor

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
- Determination of a Genomic Instability Score (GIS) through an algorithmic measurement of LOH, TAI, and LST

myChoice® CDx PLUS identifies more ovarian cancer tumors with HRD than other testing methods[1,2,3]

All High-Grade Serous Ovarian Cancer



myChoice® CDx PLUS testing identifies 2x as many patients as tumor BRCA testing and 3.5x as many as germline BRCA testing.

1. Yates et al. Annals of Oncology 2014
2. The Cancer Genome Atlas. Nature 2011
3. Moore et al.: NEJM 2018

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myChoice® CDx PLUS delivers accurate results in approximately 14 days after sample is received

Ordering physician completes the test request form (TRF).

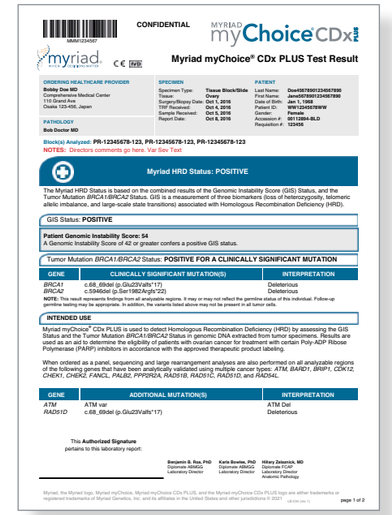
Pathologist sends tumor specimen* to Myriad laboratory.

Myriad receives the TRF and the ovarian tumor sample* and myChoice® CDx PLUS testing is performed.

Results are sent to the ordering physician.

Test result is Myriad myChoice® CDx PLUS Status which factors in both the *BRCA1/BRCA2* mutation status and the Genomic Instability Status.
A positive Tumor Mutation *BRCA1/BRCA2* Status OR a positive Genomic Instability Status (defined by a Genomic Instability Score ≥42) will lead to a final myChoice® CDx PLUS positive result.

When selected on the TRF, myChoice® CDx PLUS report will provide information on mutation status for additional 13 analytically validated HRR genes: *ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D,* and *RAD54L.*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myChoice® CDx PLUS Test Result

Myriad HRD Status: POSITIVE

GIS Status: POSITIVE

Patient Genomic Instability Score: 64

Tumor Mutation *BRCA1/BRCA2* Status: POSITIVE FOR A CLINICALLY SIGNIFICANT MUTATION

GENE	CLINICALLY SIGNIFICANT MUTATION(S)	INTERPRETATION
BRCA1	c.68_69del (p.Glu23Valfs*17)	Deleterious
BRCA2	c.5946del (p.Ser1982Argfs*22)	Deleterious

INTENDED USE

GENE	ADDITIONAL MUTATION(S)	INTERPRETATION
ATM	ATM var	ATM Del
RAD51D	c.68_69del (p.Glu23Valfs*17)	Deleterious

Example of a EU result report.

*myChoice® CDx PLUS can also be performed on breast tumors.

*myChoice® CDx PLUS is run on fixed tissues only.
Formalin Fixed Paraffin Embedded (FFPE) tumor tissues are preferred when available, however other fixatives can also be tested. Samples should ideally contain at least 30% tumor cells in tissue or fluid samples by pathologic review. Insufficient tumor DNA content in the provided tumor sample may result in a failure of the GIS Status component of the test.

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Other methods of evaluating HRD are not equivalent to myChoice® CDx PLUS

A study was done on 3,278 ovarian tumors comparing 2 methods, Myriad's proprietary Genomic Instability Status and %LOH[1]

GENOME RECONSTRUCTION

Myriad		%LOH	
Proprietary reconstruction algorithm	27,000 SNPs	**Unknown** reconstruction algorithm	3,500 SNPs

CALCULATION OF SCORES

Myriad	%LOH
Proprietary methods for calculating LOH, TAI, and LST	Proprietary method for calculating %LOH[1]

STUDY METHODS

- Tumor genomic profiles from 3,278 commercial ovarian samples were reconstructed using Myriad reconstruction algorithm
- myChoice® HRD Status was calculated using Myriad proprietary methods
- %LOH score was calculated using published method
- Comparisons were performed between Myriad's myChoice® CDx PLUS Genomic Instability Status and %LOH for the entire cohort, BRCAm only, and BRCAwt only samples

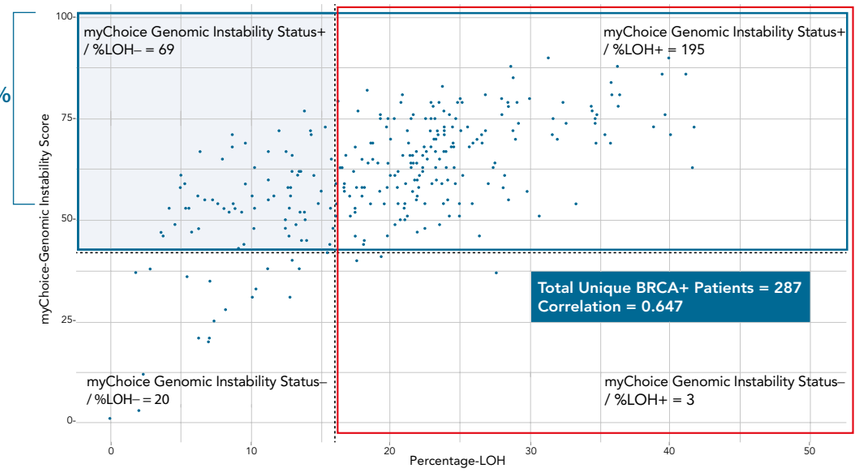
1. Mills et al. Presentation for 2020 SGO Annual Meeting. SGO Annual Meeting on Women's Cancer (Abstract 1).

myChoice® CDx PLUS identifies ~32% more tumors with HRD than %LOH alone

myChoice® Genomic Instability Status vs. %LOH[1]

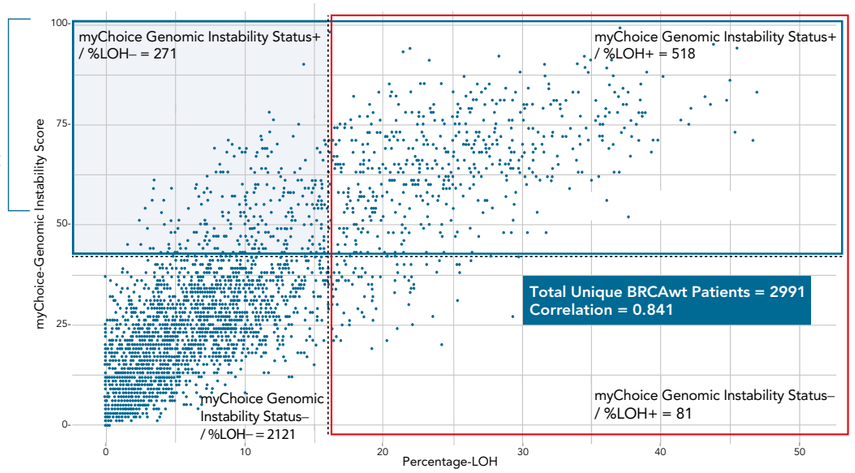
BRCA Mutant Tumors

myChoice® Genomic Instability Status identifies 92% of BRCAm samples compared to 69% identified by %LOH



BRCA Wild-type Tumors

%LOH misses 34% of samples that were identified as HR deficient by myChoice® Genomic Instability Status

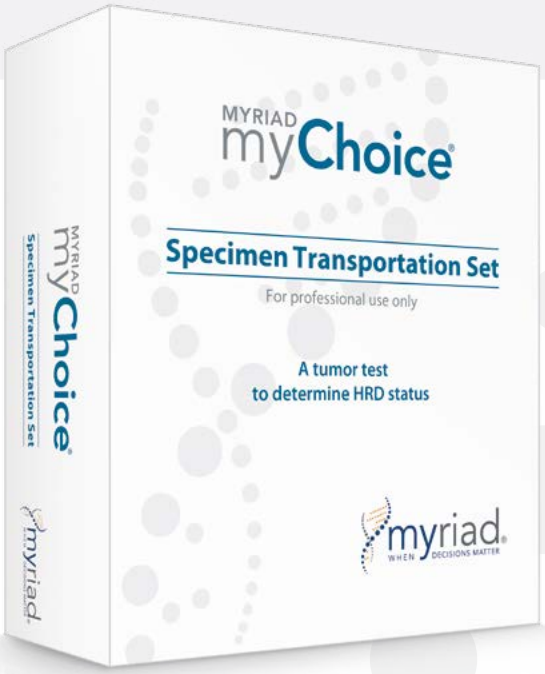


1. Mills et al. Presentation for 2020 SGO Annual Meeting. SGO Annual Meeting on Women's Cancer (Abstract 1).

myChoice® CDx PLUS can inform treatment decisions

myChoice® CDx PLUS Intended Use

Myriad myChoice® CDx PLUS is used to detect Homologous Recombination Deficiency (HRD) by assessing the Genomic Instability Status and the Tumor Mutation *BRCA1/BRCA2* Status in genomic DNA extracted from tumor specimens. Results are used as an aid to determine the eligibility of patients with ovarian cancer for treatment with certain Poly-ADP Ribose Polymerase (PARP) inhibitors in accordance with the approved therapeutic product labeling.



Analytical concordance studies have been performed with the FDA approved myChoice® CDx test.

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