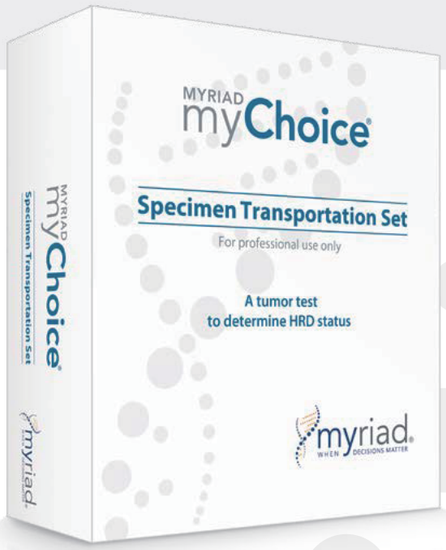
## myChoice® HRD can inform treatment decisions

### myChoice® HRD Intended Use

Myriad myChoice® HRD is used to detect Homologous Recombination Deficiency (HRD) by assessing Genomic Instability Status and Tumor Mutation Status in genomic DNA extracted from tumor specimens. This test may aid in identifying patients with positive HRD and should be used in accordance with the approved therapeutic product labeling.




The assay used for myChoice® HRD is the identical analytical assay used with the FDA approved myChoice® CDx. myChoice® CDx is the only FDA approved companion diagnostic assay for determination of both tumor BRCA1/2 status and Genomic Instability status in the US.

# MYRIAD myChoice® HRD

## The most comprehensive tumor test to determine HRD status

myChoice® is the only approved HRD assay to guide PARPi decision-making

myriad WHEN DECISIONS MATTER

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PhileKorea
Specialized in Medical & Bio Science since 2000

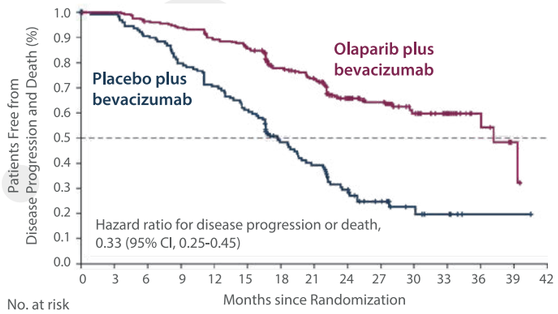
myChoice HRD_OPTIONS_BRO_07_21_EN

# First-line treatment decisions are **crucial** for women's life expectancy

## The introduction of PARP inhibitor maintenance therapy to the first-line treatment strategy provides an opportunity to extend the longest PFS interval.[1-3]

### PAOLA-1[2]

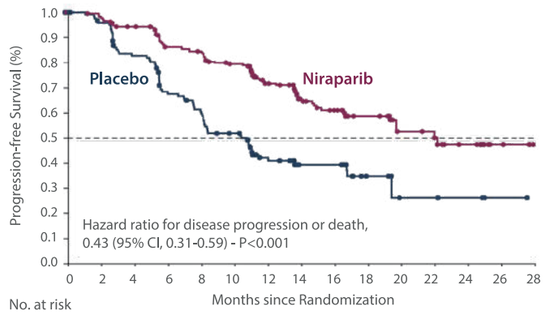
**Pre-planned analysis: patients with HRD tumors, including those with a BRCAmutation**




| No. at risk | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Olaparib plus bevacizumab | 255 | 252 | 242 | 236 | 223 | 213 | 169 | 155 | 103 | 85 | 46 | 29 | 11 | 3 | 0 |
| Placebo plus bevacizumab | 132 | 128 | 117 | 103 | 91 | 79 | 54 | 44 | 28 | 128 | 8 | 5 | 1 | 1 | 0 |

### PRIMA[3]

**Primary objective: progression-free survival in population with HRD**




| No. at risk | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Niraparib | 247 | 231 | 215 | 189 | 184 | 168 | 111 | 76 | 66 | 42 | 22 | 19 | 13 | 4 | 0 |
| Placebo | 126 | 117 | 99 | 79 | 70 | 57 | 34 | 21 | 21 | 11 | 5 | 5 | 4 | 1 | 0 |

myChoice® identifies the most appropriate patients for this first-line decision.

# GIS is the only HRD assay with front-line PARPi evidence beyond BRCA

## Validated in over 3,200 ovarian cancer patients in Phase III trials

myChoice® has been the test of choice
in 4 Phase III ovarian cancer trials for PARP inhibitors.
There are an additional 4 currently underway in 2,475 patients.

| Phase III Trial | PARPi | Study Status | n | Treatment setting |
|---|---|---|---|---|
| PAOLA-1 | Olaparib | Published | 806 | First-line |
| PRIMA | Niraparib | Published | 733 | First-line |
| VELIA | Veliparib | Published | 1140 | First-line |
| NOVA | Niraparib | Published | 553 | Recurrent |
| FIRST | Niraparib | Maturing | 912 | First-line |
| OPINION (IIIb) | Olaparib | Maturing | 279 | Recurrent |
| DUO-O | Olaparib | Recruiting | 1056 | First-line |
| OreO (IIIb) | Olaparib | Recruiting | 228 | Recurrent |

**1.** Giornelli GH 2016 **2.** Ray-Coquard et al 2019 **3.** Gonzalez-Martin et al 2019.

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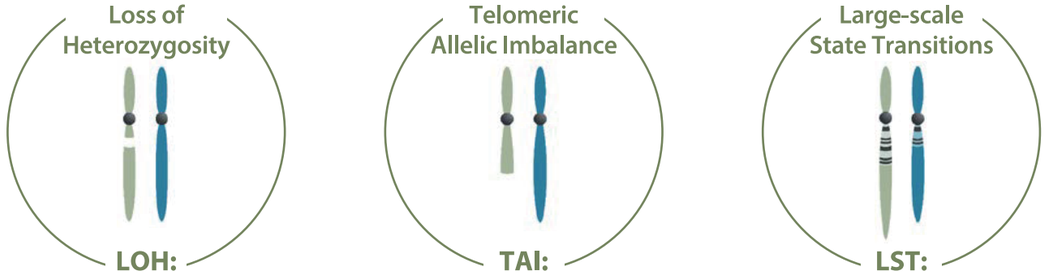
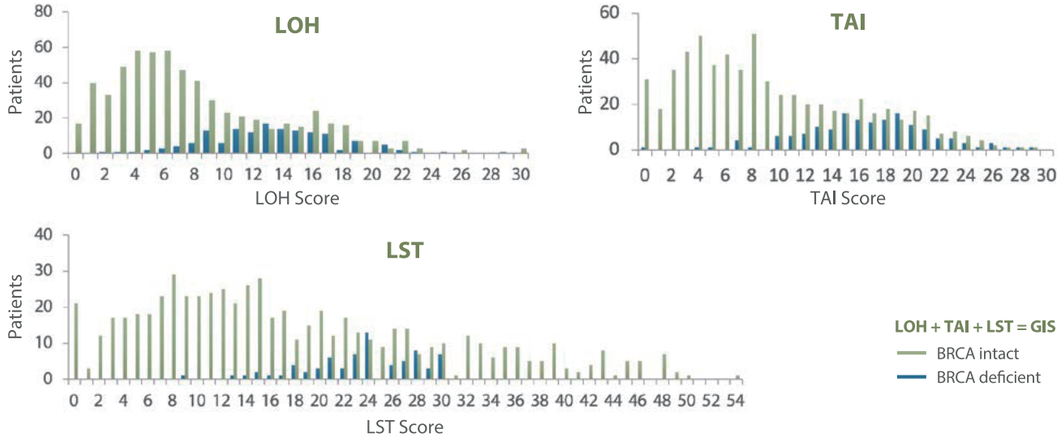
# myChoice® Genomic Instability Score (GIS) measures three HRD biomarkers (LOH, TAI, LST)

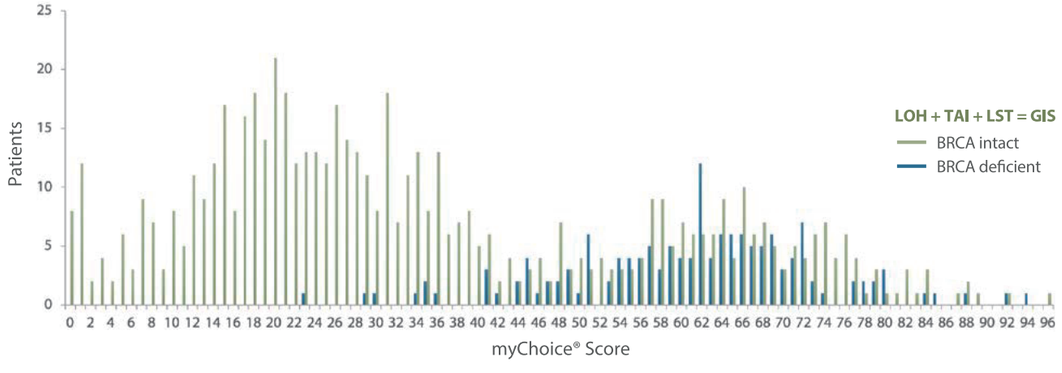



# Individual biomarkers are unable to differentiate GIS positive from negative and create a bell-curve[1]




# The combination of three biomarkers generates a bimodal distribution

## There is a high-scoring (HRD positive) and low-scoring (HRD-negative) group represented by the two peaks.




**1.** Mills et al SGO 2016

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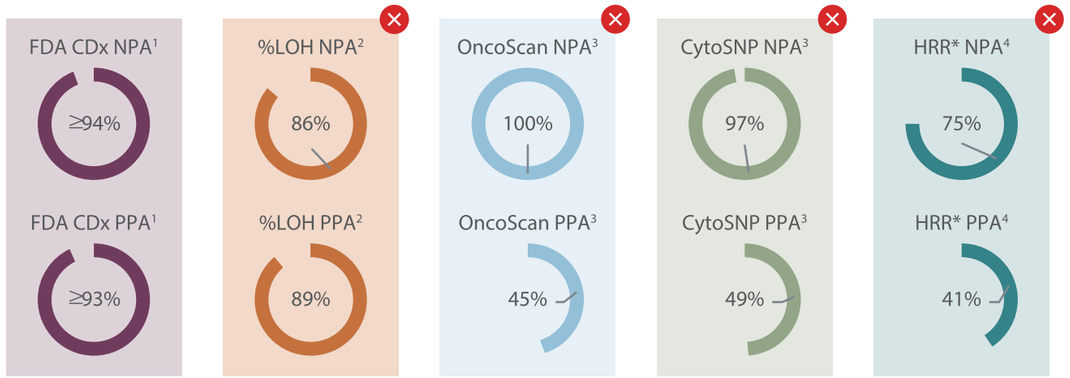
# Potential alternative Companion Diagnostics fail to reach FDA requirements for being CDx

**Where a new CDx lacks clinical evidence, FDA indicates the assay needs to be highly correlated with the original CDx. The specifications in purple reflect the minimum requirements based on the reproducibility of myChoice® HRD. New tests need to exceed both NPA and PPA minimum standards.**




*Comparison of 16 non–BRCA HRR genes vs BRCAwt PAOLA–1 patients

Each alternative HRD assay would lead to substantially less accurate treatment of patients when compared to myChoice®. Tests analysing LOH, TAI, LST (OncoScan and CytoSNP) also fail correlation.[3]

# HRD tests are not equivalent

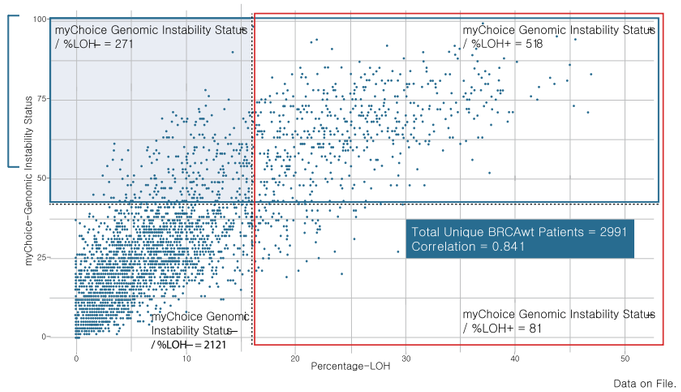
**Don't miss treatable patients with uncorrelated assays.**

A study of 3,278 ovarian tumors compares Myriad's proprietary Genomic Instability Status (GIS) and %LOH.
In the 2,991 BRCAwt patients in the study, results between the two assays had a correlation = 0.841.

**myChoice® identified ~32% more tumors with HRD.**

According to the Phase III trials PAOLA-1, PRIMA and VELIA, this patient group had significant PFS improvement compared to the control arm. Following %LOH in this study would have left these patients untreated.

**myChoice-GIS CDx Commercial Ovarian BRCA (Wildtype) Samples**




Data on File.



**1.** Li 2016 **2.** Mills et al SGO 2020 **3.** Cristescu et al ESGO 2020 **4.** Pujade–Lauraine et al SGO 2021

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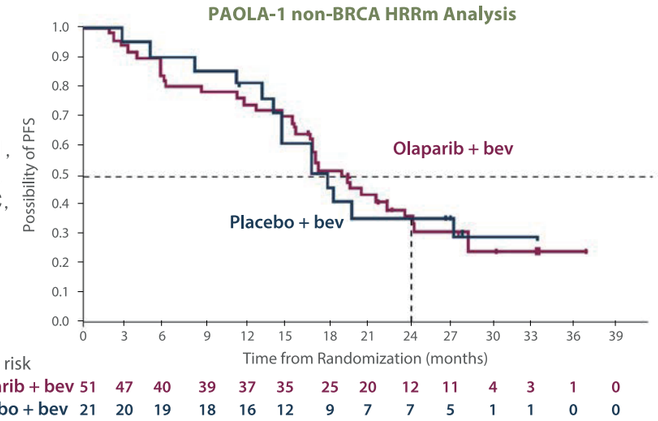
# Non-BRCA HRRm are not interchangeable with GIS and should not be considered substitutes

**As previously described by Nordquist et al 2018, non-BRCA HRR mutations are very uncommon. In this PAOLA-1 exploratory analysis, non-BRCA HRR mutations were not predictive of improved PFS.[1]**

Expanded 18-gene panel analyzed:
ATM, BARD1, BLM, BRIP1, CDK12, CHEK1, CHECK2, FANCA, FANCI, FANCL, FANCM, NBN, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D, RAD54L




MYRIAD myChoice® HRD

## Prospectively Validated[2,3,4,5]

Trusted assay for multiple clinical trials by pharmaceutical partners

## Clinically Actionable Results

Identifies patients eligible for treatment with PARP inhibitors

## International Guidelines

Include recommendations for myChoice® testing for ovarian cancer[6,7]

## Fast TAT

myChoice® HRD delivers accurate results in approx. 14 working days after sample receipt

**1.** Pujade–Lauraine et al SGO 2021 **2.** Moore et al 2018 **3.** Mirza et al 2016 **4.** Ray–Coquard et al 2019 **5.** Gonzales–Martin et al 2019 **6.** Miller et al 2020 **7.** Tew et al 2020

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# myChoice®
# is recommended by clinical guidelines

**myChoice® is the only HRD test with Level 1A evidence for first-line PARPi maintenance**

**ESMO**

**European Society of Medical Oncology**

*"In the first-line maintenance setting…use a validated scar based HRD test to establish the magnitude of benefit conferred by PARPi use"* [1]

ESMO recognizes myChoice® is the only scar based HRD test validated in the first-line maintenance setting

**ASCO**

**American Society of Clinical Oncology**

*"The addition of olaparib to bevacizumab maintenance may be offered to patients who have stage III-IV HGS or endometriod ovarian cancer and germline or somatic pathogenic or likely pathogenic variants in BRCA1 or BRCA2 genes and/or genomic instability, as determined by Myriad myChoice® CDx"* [2]

**NCCN®**

**National Comprehensive Cancer Network®**

*"Germline and/or somatic BRCA 1/2 status informs selection of maintenance therapy… In the absence of a BRCA 1/2 mutation, homologous recombination deficiency (HRD) status may provide information on the magnitude of benefit of PARP inhibitor maintenance therapy"* [3]

## International regulatory approvals for myChoice®

**FDA PMA** myChoice® CDx results are used as an aid in identifying ovarian cancer patients with positive HRD status, who are eligible, because of a positive test result in *BRCA1* or *BRCA2* genes or a positive Genomic Instability Score, for treatment with olaparib or niraparib in accordance with the approved therapeutic product labeling.

**PMDA PMA** myChoice® CDx is used to detect HRD by assessing GIS and *BRCA1/2* gene mutations in genomic DNA extracted from tumor specimens. Results are used as an aid to determine the eligibility of patients with ovarian cancer for niraparib monotherapy treatment or olaparib in combination with bevacizumab treatment. Eligibility of patients for olaparib monotherapy treatment should be based on *BRCA1/2* gene mutations only.

**CE Mark** myChoice® CDx PLUS is used to detect HRD by assessing the GIS Status and tumor *BRCA1/2* 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 PARPi in accordance with the approved therapeutic product labeling.

When ordered as a panel, sequencing and large rearrangement analyses are also performed on all analyzable regions of the following genes that have been analytically validated using multiple cancer types: *ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D,* and *RAD54L*.

**1.** Miller et al 2020 **2.** Tews et al 2020 **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer V.1.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed May 7, 2021.
To view the most recent and complete version of the guidelines, go online to NCCN.org.





MYRIAD myChoice® HRD

**BLOCKS ARE PREFERRED OVER SLIDES WHENEVER POSSIBLE**

## FOR SLIDES:

1. Please select a formalin-fixed paraffin-embedded tumor block that contains ≥40 microns of tumor. The block should contain ideally **≥30% tumor** by pathologic review with a minimum of 20%.

2. Cut and label one 5 micron section for H&E staining on a charged slide.
   Cut and label 5 micron sections on uncharged slides according to the table at right:

| Area of tumor ($mm^2$) | # of 5 µm unstained slides |
|---|---|
| 20–25 | 8 |
| 15–19 | 12 |
| 10–14 | 16 |
| 5–9 | 20 |

3. Include Test Request Form (TRF) and Pathology Report in the kit.