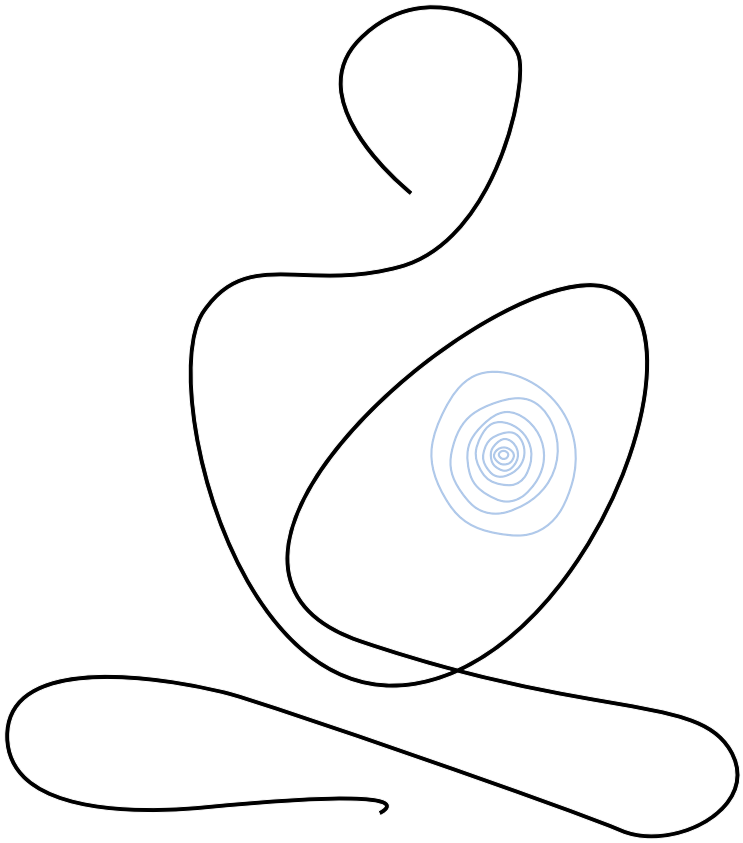
RediScore

Homologous Recombination Deficiency Score (HRD)



Genekor

Committed to Biotechnological Innovation

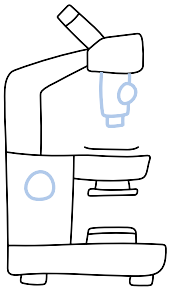
Test RediScore®

RediScore® is a test developed to predict the presence of *HRD* through the analysis of the tumor's genomic instability. It is based on the technology of SNP (*Single Nucleotide Polymotphisms)*, which is the standard method for the analysis of abnormal chromosomal structures formed as a result of the Homologous Recombination Deficiency. Combined with the analysis of alterations of the *BRCA1 & BRCA2* genes in the tumor, it gives us a **comprehensive picture of the functionality of the HR pathway.**

When is RediScore® Test Significant?

The RediScore® test is recommended for all patients with ovarian cancer, but also where the use of PARP inhibitors is under investigation for treatment or maintenance treatment of the patient.

Why is The RediScore® Test Significant?



It has now been proven by a plethora of clinical studies that about 50% of ovarian cancer patients **could benefit from the administration of PARP inhibitors.** These include patients with:

» *BRCA1/2 alterations*

» Tumors with homologous recombination deficiency (HRD)

Since 2014, four PARP inhibitors *(PARPi)* **have been approved by the FDA:** Olaparib, Niraparib, Rucaparib, and Talazoparib. **Their administration has been approved** for 4 types of cancer: ovarian, prostate, pancreatic and breast cancer.

What does HRD Mean?

HRD (Homologous Recombination Deficiency), means the inability of the cell to repair its damage through the homologous recombination pathway. The presence of genomic instability is indicative of the HR pathway insufficiency.

For the calculation of HRD, three biological parameters are used ("genomic scars"):

» **LOH** -Loss of Heterozygosity
» **TAI** - Telomeric Allelic Imbalance
» **LST** - Large Scale Transitions

BRCA1 and *BRCA2* genes play an essential role in the correct functioning of the homologous recombination. **Tumors bearing germline and / or somatic alterations in these genes have a deficiency with the homologous recombination pathway. (HRD).**

RediScore® Test Technical Characteristics

The first genomic scar-based homologous recombination deficiency (HRD) measures were produced using using the SNP microarray technology. This technology was selected since it is a reference technology for whole genome analysis of copy number to identify gains and losses as well as Loss of Heterozygosity at high genome-wide resolution.

Finally, the bioinformatics approach that was developed in Genekor, **allows high sensitivity and specificity in forecasting the HRD state.**

Tumor DNA samples from paraffin embedded tumor tissue are hybridized on the Oncoscan arrays *(Affymetrix).* Chromosome Analysis Suite (ChAS) software along with a proprietary bioinformatic algorithm is used to calculate Loss of Heterozygocity (LOH), number of telomeric-allelic imbalance (NTAI) and large-scale state transition (LST). The overall measurement of genomic instability is given as a score (GIS) and is the sum of the above three components Analysis of BRCA1/2 gene alterations and rearrangement is performed using the Oncomine technology on a S5 NGS sequencing platform.

The overall measurement of genomic instability is given as a score (GIS) and is the sum of the above three components. The analysis of alterations and of the rearrangement of the **BRCA1 / 2** genes in the tissue, is performed using Oncomine technology in Ion GeneStudio S5 sequencing platform Prime System NGS.

The determination of the Homologous Recombination Deficiency (HRD) is performed via:

» The analysis of tumor alterations in the *BRCA1 & BRCA2* genes &
» The measurement of genomic instability (GIS) throughout the genome.

Sample type / Tissue enclosed in a paraffin block
Delivery time / 15 working days

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