GIInger supports prediction of homologous recombination deficiency and patient response to PARPi treatment from shallow genomic profiles.

Pozzorini P, André G, Colletta T, et al. *Cell Rep Med.* 2023;4(12):101344. doi: 10.1016/j.xcrm.2023.101344

BACKGROUND

Homologous recombination deficiency (HRD) is a predictive biomarker for PARPi sensitivity in ovarian cancer.

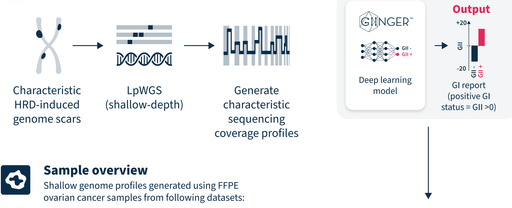
In addition to *BRCA1/2* testing, measuring genomic instability (GI) can expand identification of HRD-positive patients.

However, the complexity and centralized assessment of available solutions are **barriers to GI analysis.**

Low-pass whole genome sequencing (lpWGS) offers an easy-to-implement, decentralized HRD detection alternative.

METHODS

Sequencing overview



Sample overview

Shallow genome profiles generated using FFPE ovarian cancer samples from following datasets:

Analytical performance

5 independent clinical laboratories n=327

Clinical relevance

PARPi

PAOLA-1 clinical trial sub-cohort n=195

GIInger™ Score

Predict

HRD Status: ⊕ or ⊖

RESULTS

Analytical performance in clinical samples (n=327)

High concordance

overall percentage agreement (OPA) of GI status between GIInger™ and reference method

n = 296

Low rejection rate

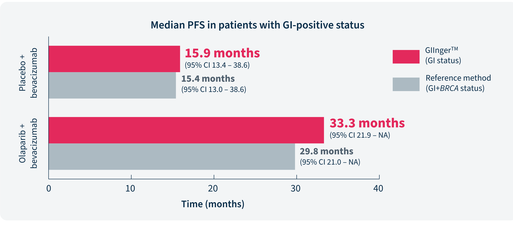
overall rejection rate with GIInger™ versus 7.95% with reference method

n = 327

No significant difference in GI status OPA was observed between samples processed across **5 independent clinical laboratories, supporting a decentralized approach to HRD analysis.**

Clinical relevance: Retrospective analysis in subset of PAOLA-1 samples (n=195)

Patients classified by GIInger™ as GI-positive had **significantly (over two times) longer progression-free survival (PFS)** when receiving olaparib + bevacizumab versus those receiving placebo + bevacizumab (hazard ratio 0.49; p=0.01).



GIInger™ classification was non-inferior to the reference method for stratifying ovarian cancer patients with regards to PARPi treatment response.

CONCLUSIONS

- GIInger™ is highly concordant with the centralized reference method for HRD assessement and shows lower rejection rate.
- GIInger™ is an easy-to-implement deep learning method that allows accurate stratification of HRD samples based on lpWGS data.
- GIInger™ can support the decentralized identification of ovarian cancer patients who may benefit from first-line maintenance treatment with PARPi.

ABBREVIATIONS

CI, confidence interval;
FFPE, formalin-fixed paraffin-embedded;
GI, genomic instability;
GII, Genomic Integrity Index;
HRD, homologous recombination deficiency;
OPA, overall percentage agreement;
PARPi, poly(ADP-ribose) polymerase 1 inhibitor;
PFS, progression-free survival.

FURTHER READING

Buisson A, Saintigny P, Constantoulakis P, et al. Blinded-assessment of a solution to evaluate olaparib maintenance treatment efficacy in patients with ovarian cancer from the GINECO/ENGOT PAOLA-1 trial. J Clin Oncol. 2023;14:5588-5588. 10.1200/JCO.2023.41.16_suppl.5588.

Pozzorini C, Andre G, Coletta C, et al. **GIInger predicts homologous recombination deficiency and patient response to PARPi treatment from shallow genomic profiles.** Cell Rep Med. 2023 Dec 19;4(12):101344. doi: 10.1016/j.xcrm.2023.101344.

GIInger™ data were generated using the SOPHiA DDM™ Dx HRD Solution, available as a CE-IVD product for In Vitro Diagnostic Use in Europe and Turkey only.

SOPHiA GENETICS products are for Research Use Only and not for use in diagnostic procedures unless specified otherwise.