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**INNOVATIVE ACADEMIC HOMOLOGOUS
RECOMBINATION DEFICIENCY TESTS
AVAILABLE IN ADVANCED OVARIAN CANCER:
THE EUROPEAN ENGOT INITIATIVE**

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Introduction Recently the PAOLA-1/ENGOT-ov25 phase-3 study (Ray-Coquard ESMO-2022) showed that the addition of olaparib maintenance to 1st-line platinum-based therapy and bevacizumab improved survival of advanced ovarian cancer (AOC) patients with HRD positive tumors independently of BRCA status (Myriad myChoice test). The aim of the European ENGOT initiative was to evaluate various academic HRD assays on PAOLA-1 tumor samples.

Methods The novel HRD tests were initially assessed on 85 samples from PAOLA-1 BRCA-wild-type patients and results were correlated with Myriad test. Subsequently, >350 PAOLA-1 samples selected on the basis of tumor DNA availability were tested. Statistics were performed independently (v26.0-SPSS). The ability of each test to predict 1st-line olaparib maintenance efficacy versus placebo was evaluated on PAOLA-1 patient progression-free survival according to HRD/BRCA status.

Results From 12/2019 to 09/2022 a total of 8 European academic laboratories representing 6 countries completed the clinical validation process on the PAOLA-1 samples. Despite the variety of methodological approaches and some differences in the distribution of HRD status, all of tests were clinically validated (table 1) and did not differ significantly from Myriad test results. Progression-free survival hazard ratio between olaparib and placebo arms depending on the assay was between 0.30 and 0.50 for HRD positive patients and between 0.88 and 1.15 for HRD negative patients.

Conclusion/Implications The ENGOT HRD initiative is a unique collaboration of European academic laboratories involved in gynaecology oncology translational research. A total of 8 innovative HRD tests achieved a clinical validation from AOC tumor samples of the phase 3 PAOLA-1 study.

Abstract PO009/#424 Table 1 HRD clinically validated tests from 8 academic laboratories and the reference myChoice Myriad HRD test

HRD assay	Affiliation	Technical sum-up	HRDpos ¹ /total No (%)	HRDpos ¹ & BRCAwt ² 0.35<HR of PFS<0.55
ICH	Humanitas University, Milano	SCNA ³ and SNV ⁴ (378 genes)	228/399 (57.1)	yes
Geneva	Geneva University Hospitals	Oncoscan SNP ⁵ assay	252/469 (53.7)	yes
ShallowHRDv2	Institut Curie, Paris	Low coverage WGS ⁶	228/449 (50.7)	yes
GIScar	Centre F. Baclesse, Caen	Instability score: 127 gene panel	258/469 (55.0)	yes
Leuven HRD	Catholic University, Leuven	NGS ⁷ SNP + gene panel	254/468 (54)	yes
Gilnger	Centre Léon Berard, Lyon	Low coverage WGS + 28 gene panel	266/469 (56.7)	yes
BRCA-like	Köln University and Netherlands Cancer Institute	Low coverage WGS	298/469 (63.5)	yes
NOGGO GIS	Berlin La Charité and Hamburg University	NGS SNP 57 gene panel	188/383 (49.1)	yes
MyChoice HRD CDx	Myriad Genetics	BRCA1/2 and GIS ⁸	242/469 (51.6)	yes

¹HRDpos: Test HRD positive; ²BRCAwt: BRCA wild type; ³SCNA: Somatic Copy Number Alteration; ⁴SNV: Single Nucleotide Variant; ⁵SNP: Single Nucleotide Polymorphism; ⁶WGS: Whole Genome Sequencing; ⁷NGS: Next-Generation Sequencing; ⁸GIS: Genomic Instability Score