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 gynecology 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.