

distribution of FOLR1 in normal tissues may increase its diagnostic and therapeutic potential through targeted agents currently under development. We characterized the FOLR1 serum expression in benign and malignant ovarian pathology pre- and postoperatively.

Methodology Patients with suspected ovarian cancer treated at our Institution between 2018-2021 were prospectively enrolled. Pre- and/or postoperative (1-8 days after) blood samples were taken. Quantitative measurement of FOLR1 serum concentration was carried out by ELISA.

Result(s)* Median age of participating patients was 53 (range 40-78). On definitive pathology 13 (22%) patients had benign adnexal masses and 46 (78%) had serous ovarian cancer. Thirty-seven (63%) patients had FIGO stage III-IV and 15 (25%) received neoadjuvant chemotherapy (NACT). Preoperative FOLR1 was significantly higher in the malignant group versus cases with benign pathology (mean 2190 ng/mL vs 499 ng/mL, $p=0.001$). NACT patients had a significantly lower preoperative FOLR1 than chemotherapy naïve patients (mean 1001 ng/mL vs 2765 ng/mL, $p=0.012$). Additionally, the preoperative FOLR1 in chemotherapy naïve patients was significantly higher in advanced-stage disease FIGO III-IV versus early-stage disease FIGO I-II (3317 ng/mL vs 1179 ng/mL, $p=0.023$). In paired pre- and postoperative samples no significant FOLR1 difference was noted ($n=19$, $p=0.64$), however for paired samples taken up to 3 days postoperatively a significant increase was seen in the postoperative value (1547 ng/mL vs 1768 ng/mL, $p=0.047$, $n=7$). Interestingly, 1/7 (14%) cases demonstrated a decrease in postoperative FOLR1 in the first 3 days while 8/12 (66.6%) cases had a decrease in postoperative FOLR1 4-8 days after ($p=0.027$).

Conclusion* Elevated serum FOLR1 values correlated with malignancy and advanced stage while NACT significantly reduced FOLR1 values, in correlation with disease burden. We describe here a significant postoperative surge of FOLR1 that decreases >3 days after surgery that requires subsequent investigation. The full diagnostic and therapeutic potential of FOLR1 is yet to be explored and further analysis in corresponding tissue samples is ongoing.

This work was supported by CNCS-UEFISCDI project PN-III-P4-PCCF-2016-0142.

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HOMOLOGOUS RECOMBINATION DEFICIENCY TESTING IN ADVANCED OVARIAN CANCER: DESCRIPTION OF THE ENGOT HRD EUROPEAN INITIATIVE

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10.1136/ijgc-2021-ESGO.356

Introduction/Background* Recently 3 Phase III first-line studies, PAOLA-1/ENGOT-ov25 (Ray-Coquard *et al.* *NEJM* 2019), PRIMA/ENGOT-ov26/GOG-3012 (Gonzales Martin *et al.* *NEJM* 2019) and VELIA/GOG-3005 (Coleman *et al.* *NEJM* 2019) have demonstrated that the addition of a PARP inhibitor (PARPi) to platinum-based therapy +/- bevacizumab improved progression-free survival (PFS) in advanced ovarian cancer (AOC) patients. The benefit was greater when the tumor was homologous recombination deficient (HRD) according to Myriad myChoice test, independently of BRCA status. The PAOLA-1 olaparib+bevacizumab maintenance regimen was approved in USA/Europe/Japan for HRD positive patients. The European initiative aims at evaluating various HRD tests on PAOLA-1 tumor samples to identify new reliable and feasible HRD tests

Methodology The HRD initiative has 2 components; one based on artificial intelligence with various partners and the other, the European HRD ENGOT initiative (EHEI), is led by academic research laboratories (RL) from ENGOT groups. The HRD test evaluation protocol for the EHEI RL includes 3 phases. The phase 1 (2019/12) brought together European RL. Because non-BRCA Homologous Recombination Repair (HRR) mutations have not been found predictive of PARPi activity in PAOLA-1 (Pujade-Lauraine *et al.*, *SGO 2021*) RL tests based on these mutations were not selected for the next phases. Phase 2 evaluated the correlation between RL tests and the Myriad myChoice test on tumor samples from 85 PAOLA-1 BRCA wild type patients using the KAPPA statistics. Phase 3 is the final PFS evaluation on more than 350 additional patient samples.

Result(s)* A total of 20 RL from 21 ENGOT groups participated to the EHEI phase 1. Half of them had a test mainly based on an HRR gene panel. Three RL did not pursue for various reasons (capacity, financial or regulatory). The remaining 7 RL from 6 countries (table 1) completed the phase 2 in May 2021 and may proceed to phase 3.

Conclusion* The EHEI is a unique collaboration of European academic laboratories involved in gynecologic oncology translational research with the aim of providing a reliable biomarker (HRD) for selecting AOC patients who could benefit most from PARPi +/- bevacizumab in first-line therapy. HRD tests performance will be described after their phase 3 is completed.

Abstract 201 Table 1 The 7 research laboratories which completed the phase 2 ENGOT European HRD initiatives

ENGOT-group (country) [¶]	Affiliation [¶]	Technical-sum-up [¶]
MANGO ⁺ (Italy) [¶]	Humanitas, Milano, Italy [¶]	WES: Scoring algorithm-based-on-the-presence-of-stretches-of-LOH, [¶]
SAKK ⁺ (Switzerland) [¶]	Geneva-University-Hospitals, [¶]	HRD-phenotype-score-based-on-whole-genome-CNVs-(ThermoFisher-OncoScan-SNP-assay) [¶]
GINECO-(France) ⁺ and-DGOG-(Netherlands) [¶]	Gustave-Roussy-and-Leiden-University-Medical-Center [¶]	Immunofluorescent-detection-of-RAD51-foci. [¶]
BGOG ⁺ (Belgium) [¶]	Catholic-University-Leuven-(KU-Leuven)-and-VIB-Centre-for-Cancer-Biology, Leuven [¶]	Capture-based-targeted-NGS-SNP-panel. [¶]
GINECO ⁺ (France) [¶]	Centre Léon Bérard, Lyon [¶]	HRD-Solution-developed-with-SOPHIA-GENETICS [¶] Targeted-sequencing-(28-genes), Low-coverage-WGS- [¶] Proprietary-Deep-learning-algorithm [¶]
AGO ⁺ (Germany) ⁺	University-of-Köln-(KU)-and-The-Netherlands-Cancer-Institute-(NKI) [¶]	BRCA1-like-copy-number-profile-based-on-low-coverage-WGS [¶]
NOGGO ⁺ (Germany) [¶]	La-Charité-(Berlin)-and-Hamburg [¶]	LOH, [¶] scarring [¶]