Submitted: 12 December, 2023 Accepted: 02 January, 2024 Published: 15 June, 2024 DOI:10.22514/ejgo.2024.042

EDITORIAL

European Journal of Gynaecological Oncology

Difficulties and inequities in access to homologous recombination deficiency testing in ovarian cancer patients

Massimo Barberis[1,*]

[1]Division of Experimental Oncology, European Institute of Oncology, IRCCS, 20139 Milano, Italy

***Correspondence**

massimo.barberis@ieo.it (Massimo Barberis)

Keywords

Ovarian cancer; HRD; Inequity; Access

According to the Global Cancer Statistics, in 2020 ovarian cancers were the eight most common malignancy in females. Their incidence accounted for 3.4% of all new cancer diagnoses in women worldwide [1]. They are the sixth most diagnosed cancer in women and the most lethal entity among all the gynecological cancers. In Italy more than 36,000 women live with this cancer; 6000 new cases are diagnosed every year and more than 3500 patients die for tumor—related causes [2]. Highgrade serous carcinoma (HGSC) is the most-common histotype of all ovarian cancers [3]. The high mortality is attributable to many factors including: non-specific and late symptoms and the absence of validated screening strategies that allow early diagnosis, except for women with alterations in *BRCA1* and *BRCA2* genes.

In women with platinum-sensitive HGSC, the introduction of Poly (ADP-ribose) polymerase inhibitors (PARPi) changed the clinical outcome both in terms of progression free and overall survival [4–7]. PARPi have the best clinical benefit in BRCA1/2 mutated cancers, but a significant efficacy can be observed in BRCA wild-type tumors with homologous recombination repair deficiency (HRD) PARPi alone or in combination with antiangiogenic therapy for mantainance therapy of HRD-positive patients [6, 7] were approved by different Agencies after the results obtained in clinical trials (Food and Drug Administration [8] and European Medicines Agency [9] in 2020, and Agenzia Italiana del Farmaco [10] in 2022).

The European Expert Consensus Recommendations [11] reported that BRCA1/2 tumor assessment should be associated with the evaluation of Homologous Recombination Repair (HRR) score to extend PARPi treatment to the largest number of patients, considering that about 20–25% of HGSCs harbor BRCA1/2 alterations and about 50% are characterized by HRD [12].

The Myriad MyChoice CDx assay, used in clinical trials that led to FDA approval of olaparib and niraparib [4, 5] is considered the gold standard test to obtain an HRD score and identify candidates for PARPi. Different studies demonstrated the feasibility and robustness of in-house testing, showing high concordances with Myriad MyChoice CDx in terms of overall, positive and negative percent agreement [13–16].

The access to HRD testing which comprises BRCA1 and BRCA2 evaluation is the only suitable tool to access to olaparib or to obtain predictive information on the potential response to other PARPi. However, in Europe there are differences in the delivery of the two tests [17]. Tumor BRCA testing is usually provided by the National Health Services with access criteria and reimbursement and pricing regimes that are not homogeneous in European countries. HRD assays, even if include the evaluation of BRCA1/2 status are generally not reimbursed. They are performed in academic or central laboratories only, the cost may be prohibitive or simply unavailable in certain countries. Currently available assays need high throughput NGS platforms and streamlined testing solutions with complex workflows that limit HRD testing to local laboratories, closer to patients. Normanno *et al.* [18] reported a survey on the access on biomarker testing proposed by European Scientific Societies, Federations of Pharmaceuticals Indrustries and Cancer Patient Associations.

The study evaluated the access to biomarker testing across Europe. The Authors reported that the access to precision medicine is higher in countries with active public reimbursement agencies. Lack of diagnostic laboratory networks, absent or inadequate public reimbursement limit the access to biomarker tests in many European countries. In countries with limited public reimbursement, pharmaceutical industry and patients' out of pocket payment were the main forms of funding for testing.

To avoid inequality and barriers the national or regional health care officers should identify the laboratories suitable to perform HRD tests, depending on the type of accreditation, the performance of the instrumentation, the staff capacity and the presence of verifiable quality assistance and quality control programs.

Only a network of laboratories that meet pre-defined struc-

tural, organizational and operative parameters can guarantee equitable access to predictive tests throughout the European countries.

This is nothing new: this is an important and proven clinical experience.

ESGO (the European Society of Gynaecological Oncology) has prepared a set of indicators for advanced ovarian cancer surgery and a consequent certification of hospital centers that offer optimal levels of surgical care. The certification is based on adherence to 10 quality indicators with a scoring evaluation system designed and validated by international experts [19].

To be eligible a centre should comply with qualitative and quantitative criteria, as defined in the ESGO curriculum that enable the fellows to gain experience in care of patients with gynaecological malignancies.

Recently, the initiative of the European Union to implement "Cancer Diagnostic and Treatment for All" identified two main barriers to access to tumour biomarkers [20].

The first is a poor awareness of the benefits of biomarker testing. The second is due to inadequate infrastructures and workforce shortage. Shortage of health care workforce in many European countries is a dramatic problem that need urgent attention [21].

In conclusion the barriers to HRD testing in ovarian cancer patients reflect the inequality in access to precision medicine based on biomarkers. The community of patients with ovarian cancer need optimal infrastructure to perform the test, development of specialized knowledge in personalized medicine, and mobilization of resources to promote equal access to high quality assays.

AVAILABILITY OF DATA AND MATERIALS

Data and materials have been obtained from my previous studies on this topic and from meetings with experts and patients' associations.

AUTHOR CONTRIBUTIONS

MB—designed the research study; performed the research; analyzed the data; wrote the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

ACKNOWLEDGMENT

Special acknowledgement to Caterina Fumagalli for previous collaborations on BRCA status in women with ovarian cancer.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians. 2021; 71: 209–249.

[2] AIOM-AIRTUM. The numbers of cancer in Italy. 2023. Available at: https://www.aiom.it/wp-content/uploads/2023/12/2023_AIOM_NDC_def.pdf (Accessed: 14 December 2023).

[3] Kim J, Park EY, Kim O, Schilder JM, Coffey DM, Cho CH, *et al*. Cell origins of high-grade serous ovarian cancer. Cancers. 2018; 10: 433.

[4] Coleman RL, Fleming GF, Brady MF, Swisher EM, Steffensen KD, Friedlander M, *et al*. Veliparib with first-line chemotherapy and as maintenance therapy in ovarian cancer. New England Journal of Medicine. 2019; 381: 2403–2415.

[5] González-Martín A, Pothuri B, Vergote I, DePont Christensen R, Graybill W, Mirza MR, *et al*. Niraparib in patients with newly diagnosed advanced ovarian cancer. New England Journal of Medicine. 2019; 381: 2391–2402.

[6] Ray-Coquard I, Pautier P, Pignata S, Pérol D, González-Martín A, Berger R, *et al*. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer. New England Journal of Medicine. 2019; 381: 2416–2428.

[7] Swisher EM, Aghajanian C, O'Malley DM, Fleming GF, Kaufmann SH, Levine DA, *et al*. Impact of homologous recombination status and responses with veliparib combined with first-line chemotherapy in ovarian cancer in the Phase 3 VELIA/GOG-3005 study. Gynecologic Oncology. 2022; 164: 245–253.

[8] LYNPARZA®. Highlights of prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/208558s013lbl.pdf (Accessed: 08 May 2020).

[9] EMA Lynparza. Summary of opinion. Post authorization. 2017. Available at: https://www.ema.europa.eu/en/documents/smop/chmp-post-authorisation-summary-positive-opinion-lynparza-ii-35-ii-36_en.pdf (Accessed: 18 September 2020).

[10] AIFA Lynparza. Reimbursement approval. 2023. Available at: https://www.aifa.gov.it/documents/20142/961234/Determina_194-2022_Lynparza.pdf (Accessed: 18 March 2022).

[11] Vergote I, González-Martín A, Ray-Coquard I, Harter P, Colombo N, Pujol P, *et al*. European experts consensus: BRCA/homologous recombination deficiency testing in first-line ovarian cancer. Annals of Oncology. 2022; 33: 276–287.

[12] Miller RE, Leary A, Scott CL, Serra V, Lord CJ, Bowtell D, *et al*. ESMO recommendations on predictive biomarker testing for homologous recombination deficiency and PARP inhibitor benefit in ovarian cancer. Annals of Oncology. 2020; 31: 1606–1622.

[13] Konstantinopoulos PA, Ceccaldi R, Shapiro GI, D'Andrea AD. Homologous recombination deficiency: exploiting the fundamental vulnerability of ovarian cancer. Cancer Discovery. 2015; 5: 1137–1154.

[14] Weichert W, Lukashchuk N, Yarunin A, Riva L, Easter A, Bannister H, *et al*. An evaluation of the performance of molecular assays to identify homologous recombination deficiency-positive tumours in ovarian cancer. International Journal of Gynecological Cancer. 2021; 31: A1–A395.

[15] Magliacane G, Brunetto E, Calzavara S, Bergamini A, Pipitone GB, Marra G, *et al*. Locally performed HRD testing for ovarian cancer? Yes, we can! Cancers. 2022; 15: 43.

[16] Fumagalli C, Betella I, Ranghiero A, Guerini-Rocco E, Bonaldo G, Rappa A, *et al*. In-house testing for homologous recombination repair deficiency (HRD) testing in ovarian carcinoma: a feasibility study comparing AmoyDx HRD Focus panel with Myriad myChoiceCDx assay. Pathologica. 2022; 114: 288–294.

[17] Kekeeva T, Andreeva Y, Tanas A, Kalinkin A, Khokhlova S, Tikhomirova T, *et al*. HRD testing of ovarian cancer in routine practice: what are we dealing with? International Journal of Molecular Sciences. 2023; 24: 10497.

[18] Normanno N, Apostolidis K, Wolf A, Al Dieri R, Deans Z, Fairley J, *et al*. Access and quality of biomarker testing for precision oncology in Europe. European Journal of Cancer. 2022; 176: 70–77.

[19] ESGO Consortium of Accreditated Centers. Requirements for ESGO accreditation & re-accreditation of European Training Centres in Gynaecological Oncology. 2023. Available at: https://esgo.org/media/2023/04/Requirements-for-Accreditation-Training-Centres-2023.pdf (Accessed: 24 April 2023).

[20] European Cancer Patient Coalition. Realising the potential of genomic technologies in cancer care. 2021. Available at: https://ecpc.org/wp-content/uploads/2021/12/Report-Realising-the-potential-of-genomic-technologies-in-cancer-care-2021.pdf. (Accessed: 07 December 2021).

[21] European Commission, Directorate-General for Employment, Social Affairs and Inclusion, McGrath J. Analysis of shortage and surplus occupations 2020, Publications Office of the European Union. 2020. Available at: https://data.europa.eu/doi/10.2767/933528 (Accessed: 28 March 2023).

How to cite this article: Massimo Barberis. Difficulties and inequities in access to homologous recombination deficiency testing in ovarian cancer patients. European Journal of Gynaecological Oncology. 2024; 45(3): 1-3. doi: 10.22514/ejgo.2024.042.