The Breast 78 (2024) 103834

Contents lists available at ScienceDirect

The Breast

journal homepage: www.journals.elsevier.com/the-breast

Olaparib monotherapy in advanced triple-negative breast cancer patients with homologous recombination deficiency and without germline mutations in *BRCA1/2*: The NOBROLA phase 2 study

Alfonso Cortés [a], Elena López-Miranda [a,b,c], Adela Fernández-Ortega [d], Vicente Carañana [e], Sonia Servitja [f], Ander Urruticoechea [g], Laura Lema-Roso [h], Antonia Márquez [i], Alexandros Lazaris [b,c], Daniel Alcalá-López [b,c], Leonardo Mina [b,c], Petra Gener [b,c], Jose Rodríguez-Morató [b,c], Gabriele Antonarelli [j,k], Antonio Llombart-Cussac [b,c,e,*], José Pérez-García [b,c,l], Javier Cortés [b,c,l,m]

[a] *Hospital Universitario Ramón y Cajal, Madrid, Spain*
[b] *Medica Scientia Innovation Research (MEDSIR), Barcelona, Spain*
[c] *Medica Scientia Innovation Research (MEDSIR), Ridgewood, New Jersey, USA*
[d] *Institut Català d' Oncologia L'Hospitalet (ICO) L'Hospitalet, Barcelona, Spain*
[e] *Department of Medical Oncology, Hospital Arnau de Vilanova, Valencia, Spain*
[f] *Hospital del Mar, Barcelona, Spain*
[g] *Gipuzkoa Cancer Unit- Osakidetza/Biodonostia, San Sebastián, Spain*
[h] *Hospital Universitario 12 de Octubre, Madrid, Spain*
[i] *UGCI Oncología Médica, Hospital Universitario Regional y Virgen de la Victoria, IBIMA, Málaga, Spain*
[j] *Department of Oncology and Haemato-Oncology (DIPO), University of Milan, Milan, Italy*
[k] *Division of Early Drug Development for Innovative Therapy, European Institute of Oncology, IRCCS, Milan, Italy*
[l] *International Breast Cancer Center (IBCC), Pangaea Oncology, Quiron Group, Barcelona, Spain*
[m] *Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain*

ARTICLE INFO

Keywords:
Triple-negative breast cancer
PARP inhibitors
Olaparib
Germline BRCA1/2 mutations
Homologous recombination deficiency

ABSTRACT

Purpose: To evaluate olaparib in advanced triple negative breast cancer (TNBC) patients with homologous recombination deficiency (HRD) and no germline *BRCA1/2* mutations (g*BRCA1/2*mut).
Methods: NOBROLA (NCT03367689) is a single-arm, open-label, multicenter, phase IIa trial, enrolling adult patients with advanced TNBC without *gBRCA1/2mut* and with HRD, who were treated with olaparib. The primary endpoint was clinical benefit rate (CBR) per RECIST v.1.1.
Results: Six of 114 patients were eligible and received olaparib. Median follow up was 8.5 months. CBR and overall response rate (ORR) were 50 % (95 % CI, 11.8–88.2).
Conclusions: The observed results could prompt further investigation.
Trial: ClinicalTrials.gov identifier NCT03367689.

1. Introduction

Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer (BC) that represents 10–20 % of BC cases [1,2]. TNBC, defined by lack of tumor cell expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) [3], exhibits increasing tumor heterogeneity [4] and genomic instability, which can be caused by homologous recombination deficiency (HRD) [1,5]. HRD can result from germline mutations in *BRCA1/2* genes, as well as somatic *BRCA1/2* mutations or germline mutations in other genes involved in homologous recombination repair (HRR), found in 10–15 % and less than 4 % of TNBC, respectively [6,7]. Loss-of-function mutations in HRR genes sensitise tumors to poly (ADP-ribose) polymerase inhibitors (PARPi) [8,9]. In TNBC, PARPi are approved for patients with germline *BRCA1/2* mutations (g*BRCA1/2*-mut) [2,10]; however, HRD tumors without g*BRCA1/2mut* display

* Corresponding author. Department of Medical Oncology, Hospital Arnau de Vilanova, Valencia, Spain.
E-mail address: antoniollombart@medsir.org (A. Llombart-Cussac).

https://doi.org/10.1016/j.breast.2024.103834
Received 29 July 2024; Received in revised form 1 November 2024; Accepted 2 November 2024
Available online 3 November 2024
0960-9776/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

synthetic lethality with PARPi [11–16]. The NOBROLA trial aimed to evaluate the activity of olaparib monotherapy in advanced TNBC patients with HRD and without g*BRCA1/2*mut.

2. Material and methods

2.1. Study design

NOBROLA (NCT03367689) was a single-arm, open-label, multicenter phase IIa trial conducted across 17 Spanish sites enrolling adult patients with advanced TNBC without g*BRCA1/2*mut and HRD, determined by Myriad myChoice® HRD Plus CDx or FoundationOne® CDx tests. Detailed eligibility criteria are provided in Supplementary Material.

This study was performed in agreement with the Declaration of Helsinki and Good Clinical Practice guidelines and was approved by Institutional Review Boards or independent ethics committees at each site. All patients provided written informed consent.

2.2. Procedures

Patients received 300 mg of olaparib orally, twice daily, throughout 28-day cycles until disease progression, symptomatic deterioration, unacceptable toxicity, death, withdrawal of consent, or study completion, whichever occurred first. Detailed procedures are reported in Supplementary Material.

2.3. Outcomes

The primary endpoint was clinical benefit rate (CBR), assessed by investigators as per RECIST v.1.1. Secondary efficacy and safety outcomes are detailed in Supplementary Material.

2.4. Statistical analysis

Statistical analyses are detailed in Supplementary Material.

3. Results

Between April 2018 and December 2021, 114 patients were screened and only six received olaparib (Fig. 1, Table 1). The study was prematurely terminated because of slow accrual.

All patients were women, with a median age of 60 (range, 45–76) years and received up to three prior lines of treatment in the advanced setting. Baseline characteristics are in Table 2. By November 24, 2022, median follow-up time was of 8.5 months (range, 4.2–34.4). All patients discontinued treatment because of disease progression. At data cutoff, one patient was alive, four had died, and one was lost to follow-up 6 months after the study beginning. Three patients achieved partial responses for a CBR at 24 weeks of 50 % (95 % CI, 11.8–88.2) among 6 patients and an overall response rate (ORR) of 50 % (95 % CI, 11.8–88.2) (Table 3).

Median time to response was 1.9 months (95 % CI, 1.8–3.6) and median duration of response was 4.9 months (95 % CI, 4.7–13.2). Median progression-free survival was 6.2 months (95 % CI, 0.8–15.1) and median overall survival was 19.4 months (95 % CI, 4.2–34.4) (Supplementary Fig. 1).

Treatment-emergent adverse events (TEAEs) were grade 1–2 (5 [83.3 %] events). Grade 3 TEAEs occurred in 66.6 % patients, being anemia the most frequent (33 %). There were no grade 4 TEAEs (Supplementary Table 1). The most common TEAEs of any grade were anemia (83 % patients), and fatigue (50 % patients). All TEAEs are shown in Supplementary Table 2. Any patient experienced serious TEAEs related to olaparib. No treatment-related deaths occurred.

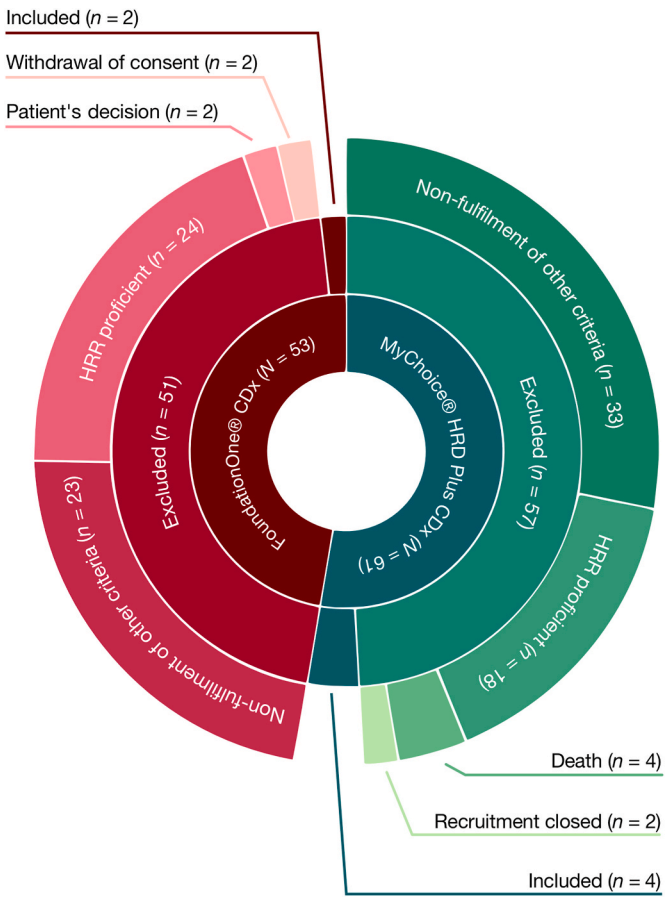

Fig. 1. Patient disposition.

4. Discussion

The NOBROLA phase II trial showed antitumor activity of olaparib monotherapy in 50 % of advanced TNBC patients with HRD and without g*BRCA1/2mut*, a rare group of patients with limited treatment options and who have not been considered in previous clinical trials.

Tumors with g*BRCA1/2*mut in the homologous recombination pathway are significantly prevalent in TNBC and associated with response to PARPi [11,16]; however, PARPi also have activity in tumors beyond g*BRCA1/2*mut [17]. The Talazoparib Beyond BRCA phase II trial reported 54 % CBR in patients with mutations in genes different from *BRCA1/2* [12]. Similarly, the TBCRC 048 phase II trial demonstrated 50 % CBR with olaparib in BC patients with germline non-*BRCA1/2* [14]. The PETREMAC phase II study achieved 51.9 % ORR using olaparib in TNBC without germline *BRCA1/2* and *PALB2* mutations [18]. Apart from the small sample size, clinical responses observed in our study may probably occur because HRD is associated with response to PARPi, even independently of the BRCA1/2 status [19], and other HRD-related genes beyond *BRCA1/2* may be sensitive to these treatments [20].

NOBROLA was a non-randomized trial in which low frequency of HRD cases was detected after more than 100 analyses and, therefore, the trial was closed earlier than expected. Most of screened subjects had no relevant alterations in the HRD-related genes. HRD can result from deleterious mutations in HRR genes in a very low percentage of TNBC patients [6,7]. *BRCA1/2* mutations are the most common mutations to cause HRD [21]; however, mutations in other HRD-related genes (such as RAD51 or ATM) may occur, although these events are less frequent [21–23]. Altogether, this may explain the low incidence of HRD cases in the screened population. The results of this study must be interpreted with caution due to some limitations, which included (a) the

Table 1
Patient disposition.

Parameter	n (%) N = 114
Patients tested with FoundationOne® CDx	53 (46.5)
Included	2 (3.8)
Excluded	51 (96.2)
Patient's decision	2 (3.8)
Withdrawal of consent	2 (3.8)
Non-fulfilment of inclusion criteria	47 (88.7)
HRD negative[a]	24 (45.3)
Inadequate or unavailable tissue sample	7 (13.2)
Disease progression to a prior platinum-based treatment	11 (20.7)
Hormone receptor status[b]	3 (5.7)
Non-measurable disease only	1 (1.9)
Number or type of prior lines of treatment	1 (1.9)
Patients tested with Myriad myChoice® HRD Plus CDx	61 (53.5)
Included	4 (6.6)
Excluded	57 (93.4)
Death	4 (6.6)
Recruitment closed	2 (3.3)
Non-fulfilment of inclusion criteria	51 (83.6)
HRD negative[a]	18 (29.5)
Inadequate or unavailable tissue sample	13 (21.3)
Disease progression to a prior platinum-based treatment	10 (16.4)
Number or type of prior lines of treatment	7 (11.5)
ECOG PS $\geq$ 2	1 (1.6)
Non-measurable disease only	1 (1.6)
Hormone receptor status	1 (1.6)

Percentages may not add up to 100 because of rounding.
Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; HRD, homologous recombination deficiency.
[a] HRD negative indicates either no relevant alteration in any HRD-related genes (FoundationOne® CDx test) or a score <33 (Myriad myChoice® HRD Plus CDx test).
[b] Logistic issues led to 3 patients receiving delayed results.

Table 2
Baseline patient characteristics.

Baseline characteristics	n (%) N = 6
Age; median (min; max) (years)	60 (45; 76)
Sex	
Female	6 (100)
Male	0 (0)
Disease status	
Locally advanced disease	0 (0)
Metastatic disease	6 (100)
ECOG PS	
0	2 (33)
1	4 (67)
Measurable disease	
Yes	6 (100)
No	0 (0)
Number of target lesions	
1	3 (50)
2	1 (17)
3	2 (33)
Metastatic sites	
Bone	1 (17)
Brain	1 (17)
Liver	1 (17)
Lung	2 (33)
Lymph nodes	2 (33)
Previous treatment for early disease	
Yes	6 (100)
No	0 (0)
(Neo)adjuvant treatment for early disease	
Taxane	6 (100)
Platinum	6 (100)
Anthracycline	6 (100)
Cyclophosphamide	6 (100)
Anastrozole	1 (17)
Trastuzumab	1 (17)
Fluorouracil	1 (17)
Others	6 (100)
Number of previous lines of therapy for ABC	
1	1 (17)
2	2 (33)
3	3 (50)
Previous treatment for ABC	
Taxane	6 (100)
Platinum	1 (17)
Anthracycline	1 (17)
Capecitabine	5 (83)
Eribulin	1 (17)
Gemcitabine	1 (17)
Targeted therapy	3 (50)
Atezolizumab	1 (17)
Others	6 (100)

Abbreviations: ABC, advanced breast cancer; ECOG PS, Eastern Cooperative Oncology Group performance status.

heterogeneous definition of the HRD status, which is related to differences in the methods used to assess HRD, the biological complexity of HRR pathways, and the types of genomic alterations evaluated [24], (b) the slow patient accrual rate due to the low incidence of HRD cases and, consequently, (c) the small sample size and limited dataset, which weakened the statistical power of the results and precluded several planned analyses.

This only prompts more data and more relevant selection criteria. The low incidence in this population presents a significant challenge that limits conducting studies with a large sample size. If results from future trials were similar, entities should reconsider the approval of new drugs in infrequent patient populations without requiring pivotal phase III studies.

5. Conclusions

Olaparib provided antitumor activity in 50 % of patients. These results warrant further investigation in larger trials.

CRediT authorship contribution statement

Alfonso Cortés: Writing – original draft, Validation, Supervision, Investigation. **Elena López-Miranda:** Writing – original draft, Validation, Supervision, Resources, Investigation. **Adela Fernández-Ortega:** Writing – original draft, Validation, Supervision, Resources, Project administration, Investigation. **Vicente Carañana:** Writing – original draft, Validation, Supervision, Resources, Investigation. **Sonia Servitja:** Writing – original draft, Validation, Supervision, Investigation. **Ander Urruticoechea:** Writing – original draft, Validation, Supervision, Investigation. **Laura Lema-Roso:** Writing – original draft, Validation, Supervision, Resources, Investigation. **Antonia Márquez:** Writing – original draft, Validation, Supervision, Resources, Investigation. **Alexandros Lazaris:** Writing – original draft, Validation, Resources, Project administration. **Daniel Alcalá-López:** Writing – original draft, Formal analysis, Data curation. **Leonardo Mina:** Writing – original draft, Formal analysis, Data curation. **Petra Gener:** Writing – original draft, Validation. **Jose Rodríguez-Morató:** Writing – original draft, Validation. **Gabriele Antonarelli:** Writing – original draft, Validation, Investigation. **Antonio Llombart-Cussac:** Writing – original draft, Validation, Supervision, Investigation, Funding acquisition, Conceptualization. **José Pérez-García:** Writing – original draft, Validation, Supervision, Investigation, Conceptualization. **Javier Cortés:** Writing – original draft, Validation, Supervision, Investigation, Funding acquisition, Conceptualization.

Data sharing statement

Data collected within the NOBROLA study will be made available to researchers upon revision and approval based on scientific merit by the trial management group (which includes a qualified statistician) of a detailed proposal for their use. The data required for the approved,

Table 3
Efficacy analyses (per RECIST v1.1) assessed by investigators.

CBR	ORR	BOR	TTR (months)	DOR (months)	PFS		OS	
					Months	Event	Months	Event
Individual patient data								
Yes	Yes	PR	3.6	4.7	8.3	PD	12.0	No
Yes	Yes	PR	1.8	13.2	15.1	PD	19.5	Death
Yes	Yes	PR	1.9	4.9	7.0	PD	7.8	Death
No	No	SD < 24W			3.5	PD	34.4	Death
No	No	PD			1.0	PD	4.3	Death
No	No	SD < 24W			5.4	PD	6.7	Loss to FU
Global data*								
50 (11.8–88.2)			1.9 (1.8–3.6)	4.9 (4.7–13.2)	6.2 (0.8–15.1)		19.4 (4.2–34.4)	

Abbreviations:BOR: Best Overall Response; CBR: Clinical Benefit Rate; DOR: Duration Of Response; FU: Follow-Up; ORR: Overall Response Rate; OS: Overall Survival; PD: Progressive Disease; PFS: Progression-Free Survival; PR: Partial Response; SD: Stable Disease; TTR: Time to response; W: Weeks.

* The values in parentheses for CBR, ORR, PFS, and OS are expressed as 95% confidence intervals. The values in parentheses for TTR and DOR are expressed as minimum and maximum.

specified purposes and the trial protocol will be provided after the completion of a data-sharing agreement that will be set up by the study sponsor. All data provided are anonymized to respect the privacy of patients who have participated in the trial in line with applicable laws and regulations.

Declaration of competing interest

AC declares consulting or advisory role (GSK, AZ, Pfizer, and Daiichi Sankyo), speaker's bureau (GSK, AZ, MSD, Clovis, and Accord), research funding (Pfizer, and GSK), travel expenses (Daiichi Sankyo, and Pfizer), and other relationships (Co-founder ONCAR). **EL-M** declares consultant or advisory board role (Roche, AstraZeneca, and Daiichi Sankyo), and travel expenses (Roche, and Gilead). **SS** declares speakers' bureau (Daiichi-Sankyo, AstraZeneca, RocheO, and Novartis), advisory board role (Seagen, Genomic Health, MSD, and Daiichi-Sankyo) and travel expenses (Daiichi-Sankyo). **AL, DA-L, LM, PG, and JR-M** declare to be employees at Medica Scientia Innovation Research (MEDSIR). **GA** declares honoraria from Medica Scientia Innovation Research (MEDSIR). **AL-C** declares research support (Roche, Agendia, Lilly, Pfizer, Novartis, Merck Sharp & Dohme, Gilead, and Daichii-Sanyo), consulting or advisory role (Lilly, Roche, Pfizer, and Novartis). speakers' bureaus (Lilly, AstraZeneca, and Merck Sharp & Dohme), travel expenses (Roche, Pfizer, and AstraZeneca), and stock or other ownership (MEDSIR and Initia-Research). **JP-G** declares advisory role (Lilly, Roche, Eisai, Daichii Sankyo, AstraZeneca, Seattle Genetics, and Gilead). travel expenses (Roche) and employment (MEDSIR). **JC** declares consulting or advisory role (Roche, Celgene, Cellestia, AstraZeneca, Seattle Genetics, Daiichi Sankyo, Erytech, Athenex, Polyphor, Lilly, Merck Sharp&Dohme, GSK, Leuko, Bioasis, Clovis Oncology, Boehringer Ingelheim, Ellipses, Hibercell, BioInvent, Gemoab, Gilead, Menarini, Zymeworks, Reveal Genomics, Expres2ion Biotechnologies), honoraria (Roche, Novartis, Celgene, Eisai, Pfizer, Samsung Bioepis, Lilly, Merck Sharp&Dohme, Daiichi Sankyo, Astrazeneca), research funding to the Institution (Roche, Ariad pharmaceuticals, AstraZeneca, Baxalta GMBH/Servier Affaires, Bayer healthcare, Eisai, F. Hoffman-La Roche, Guardanth health, Merck Sharp&Dohme, Pfizer, Piqur Therapeutics, Puma C, Queen Mary University of London), Stock (MedSIR, Nektar Pharmaceuticals, Leuko [relative]), Travel, accommodation, expenses (Roche, Novartis, Eisai, Pfizer, Daiichi Sankyo, AstraZeneca, Gilead), and patents (Pharmaceutical Combinations of A Pi3k Inhibitor And A Microtubule Destabilizing Agent. Javier Cortés Castán, Alejandro Piris Giménez, Violeta Serra Elizalde. WO 2014/199294 A. ISSUED; Her2 as a predictor of response to dual HER2 blockade in the absence of cytotoxic therapy. Aleix Prat, Antonio Llombart, Javier Cortés.US 2019/0338368 A1_LICENSED). **AF-O, VC, AU, LL-R,** and **AM** declare no conflicts of interests.

Acknowledgements

This study was funded by AstraZeneca, who did not participate in data collection, data analysis, data interpretation, or writing of this report. We thank the patients and their caregivers for participating in this study, as well as the trial teams at the participating sites and the trial unit at MEDSIR. The authors thank Angela Rynne Vidal, PhD, and Valeria Di Giacomo, PhD, from ThePaperMill, for providing writing support, funded by MEDSIR.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2024.103834.

References

[1] Bianchini G, De Angelis C, Licata L, Gianni L. Treatment landscape of triple-negative breast cancer — expanded options, evolving needs. Nat Rev Clin Oncol 2022 Feb;19(2):91–113.
[2] Gennari A, André F, Barrios CH, Cortés J, de Azambuja E, DeMichele A, et al. ESMO Clinical Practice Guideline for the diagnosis, staging and treatment of patients with metastatic breast cancer. Ann Oncol 2021 Dec;32(12):1475–95.
[3] Derakhshan F, Reis-Filho JS. Pathogenesis of triple-negative breast cancer. Annu Rev Pathol 2022 Jan 24;17:181–204.
[4] Zhou S, Huang YE, Liu H, Zhou X, Yuan M, Hou F, et al. Single-cell RNA-seq dissects the intratumoral heterogeneity of triple-negative breast cancer based on gene regulatory networks. Mol Ther Nucleic Acids 2021 Mar 5;23:682–90.
[5] van der Noord VE, van de Water B, Le Dévédec SE. Targeting the heterogeneous genomic landscape in triple-negative breast cancer through inhibitors of the transcriptional machinery. Cancers 2022 Sep 7;14(18):4353.
[6] Couch FJ, Hart SN, Sharma P, Toland AE, Wang X, Miron P, et al. Inherited mutations in 17 breast cancer susceptibility genes among a large triple-negative breast cancer cohort unselected for family history of breast cancer. J Clin Oncol 2015 Feb 1;33(4):304–11.
[7] Shimelis H, LaDuca H, Hu C, Hart SN, Na J, Thomas A, et al. Triple-negative breast cancer risk genes identified by multigene hereditary cancer panel testing. J Natl Cancer Inst 2018 Aug 1;110(8):855–62.
[8] Belli C, Duso BA, Ferraro E, Curigliano G. Homologous recombination deficiency in triple negative breast cancer. Breast 2019 Jun;45:15–21.
[9] Paulet L, Trecourt A, Leary A, Peron J, Descotes F, Devouassoux-Shisheboran M, et al. Cracking the homologous recombination deficiency code: how to identify responders to PARP inhibitors. Eur J Cancer Oxf Engl 1990. 2022 May;166:87–99.
[10] Gradishar WJ, Moran MS, Abraham J, Abramson V, Aft R, Agnese D, et al. NCCN Guidelines® insights: breast cancer, version 4.2023: featured updates to the NCCN guidelines. J Natl Compr Cancer Netw 2023 Jun;21(6):594–608.
[11] Litton JK, Rugo HS, Ettl J, Hurvitz SA, Gonçalves A, Lee KH, et al. Talazoparib in patients with advanced breast cancer and a germline BRCA mutation. N Engl J Med 2018 Aug 23;379(8):753–63.
[12] Gruber JJ, Afghahi A, Timms K, DeWees A, Gross W, Aushev VN, et al. A phase II study of talazoparib monotherapy in patients with wild-type BRCA1 and BRCA2 with a mutation in other homologous recombination genes. Nat Cancer 2022 Oct 17;3(10):1181–91.
[13] Smith MR, Scher HI, Sandhu S, Efstathiou E, Lara PN, Yu EY, et al. Niraparib in patients with metastatic castration-resistant prostate cancer and DNA repair gene defects (GALAHAD): a multicentre, open-label, phase 2 trial. Lancet Oncol 2022 Mar;23(3):362–73.

[14] Tung NM, Robson ME, Ventz S, Santa-Maria CA, Nanda R, Marcom PK, et al. TBCRC 048: phase II study of olaparib for metastatic breast cancer and mutations in homologous recombination-related genes. J Clin Oncol 2020 Dec 20;38(36): 4274–82.
[15] Mateo J, Porta N, Bianchini D, McGovern U, Elliott T, Jones R, et al. Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial. Lancet Oncol 2020 Jan;21(1):162–74.
[16] Robson M, Im SA, Senkus E, Xu B, Domchek SM, Masuda N, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. N Engl J Med 2017 Aug 10;377(6):523–33.
[17] Xu Q, Li Z. Update on poly ADP-ribose polymerase inhibitors in ovarian cancer with non-BRCA mutations. Front Pharmacol 2021;12:743073.
[18] Eikesdal HP, Yndestad S, Elzawahry A, Llop-Guevara A, Gilje B, Blix ES, et al. Olaparib monotherapy as primary treatment in unselected triple negative breast cancer. Ann Oncol Off J Eur Soc Med Oncol 2021 Feb;32(2):240–9.
[19] How JA, Jazaeri AA, Fellman B, Daniels MS, Penn S, Solimeno C, et al. Modification of homologous recombination deficiency score threshold and association with long-term survival in epithelial ovarian cancer. Cancers 2021 Feb 24;13(5):946.
[20] Ryan A, Cruz SM, Miller R, Kristeleit R. PARP inhibitor (PARPi) monotherapy treatment in non-BRCA and/or non-serous gynaecological cancers. Ann Oncol 2018 Sep;29:vi34.
[21] Chai Y, Chen Y, Zhang D, Wei Y, Li Z, Li Q, et al. Homologous recombination deficiency (HRD) and BRCA 1/2 gene mutation for predicting the effect of platinum-based neoadjuvant chemotherapy of early-stage triple-negative breast cancer (TNBC): a systematic Review and meta-analysis. J Personalized Med 2022 Feb 21;12(2):323.
[22] Furlanetto J, Möbus V, Schneeweiss A, Rhiem K, Tesch H, Blohmer JU, et al. Germline BRCA1/2 mutations and severe haematological toxicities in patients with breast cancer treated with neoadjuvant chemotherapy. Eur J Cancer 2021 Mar;145: 44–52.
[23] Holanek M, Selingerova I, Bilek O, Kazda T, Fabian P, Foretova L, et al. Neoadjuvant chemotherapy of triple-negative breast cancer: evaluation of early clinical response, pathological complete response rates, and addition of platinum salts benefit based on real-world evidence. Cancers 2021 Mar 30;13(7):1586.
[24] Stewart MD, Merino Vega D, Arend RC, Baden JF, Barbash O, Beaubier N, et al. Homologous recombination deficiency: concepts, definitions, and assays. Oncol 2022 Mar 11;27(3):167–74.