BMC Cancer

RESEARCH Open Access

Talazoparib in patients with BRCA mutant metastatic breast or ovarian carcinoma: results of early access program

Mehmet Ali Nahit Sendur[1,2*†], Mutlu Hizal[2*†], Burcu Çakar[3], Oktay Halit Aktepe[4], Emrah Eraslan[5], Zafer Arık[6], İsmail Erturk[7], Sercan Aksoy[6], Semra Paydaş[8], Serkan Değirmencioğlu[9], Cihan Erol[1], Necla Demir[10], Gülcan Bulut[11], Naziye Ak[12], Metin Özkan[13], Alper Sevinç[14], Nuriye Özdemir[15], Umut Dişel[16], Deniz Tural[17], Mehmet Artaç[18], Hacı Mehmet Türk[19], Serkan Menekşe[20], Sema Sezgin Göksu[21], Fatih Köse[22], Cağlayan Geredeli[23], Meral Günaldı[24], Başak Oyan Uluç[25], Fatma Şen[26], Kerem Oruç[27], Ömer Fatih Ölmez[28], Abdullah Sakin[28], Umut Demirci[29], Dilek Erdem[30], Ferhat Ekinci[31], Nihat Ökten[32], Leyla Özer[33], Kerem Okutur[34], Atakan Demir[25], Nuri Karadurmuş[7], Muhammed Bülent Akıncı[1], Bülent Yalçın[1] and Erhan Gökmen[3]

Abstract

Introduction Talazoparib is a strong PARP inhibitor with significant catalytic inhibition as well as the ability to cause PARP entrapment at DNA damage sites. It is one of the recommended treatments for individuals with BRCA-mutant advanced breast cancer, although research on its efficacy in advanced ovarian cancer is limited. The purpose of this study was to evaluate the efficacy of talazoparib in advanced breast and ovarian cancer patients with BRCA mutations.

Materials and methods Patients with advanced breast (HR + or TNBC) and ovarian cancer who had germline BRCA mutations were included in this multicenter, retrospective study. There were no exclusion criteria regarding treatment-line, metastatic sites or performance status. All patients received talazoparib treatment via early-access programme. The primary endpoint was PFS. Secondary endpoints were OS and ORR.

Results There were 47 and 42 patients in the breast cancer (BC) and ovarian cancer (OC) cohorts, respectively. In BC cohort, after median 13.6 months follow-up the median PFS was 6.5 months (5.0–8.1 months, 95% CI). In this heavily pretreated cohort, the ORR was 31.9% and the estimated 12-month OS rate was 73.6%. In OC cohort, the median follow up period was 13.7 months and the median PFS was 9.1 months (7.3–10.8 months, 95% CI). The ORR was 47.6% and the estimated 12-month OS rate was 75.9% in OC patients.

†Mehmet Ali Nahit Sendur and Mutlu Hizal are co-first author of this paper.

*Correspondence:
Mehmet Ali Nahit Sendur
masendur@yahoo.com.tr
Mutlu Hizal
drmutluhizal@hotmail.com

Full list of author information is available at the end of the article

Conclusion Talazoparib may be an effective therapy option for patients with advanced BRCA-mutant breast cancer. In the absence of prospective phase 2/3 data, the outcomes of OC cohort may also considerably contribute to the literature on BRCA-mutant ovarian cancer.

Introduction

The poly(adenosine diphosphate-ribose) polymerase (PARP) protein family is essential for cell function, particularly DNA repair and apoptosis. The crucial role they play in the repair of single-strand DNA breaks provides a basis for targeted treatment [1]. Patients with mutations in breast cancer susceptibility genes (BRCA) have genomic instability because they are unable to repair double-strand DNA breaks. In this patient population, whose homologous recombination (HR) function is already diminished, PARP inhibition causes DNA to become irreparable. This so-called "synthetic lethality" leads to the cell death [1].

Mutations in BRCA1 and BRCA2 may contribute to the development of several cancer types [2]. Thus, PARP inhibitors (PARPi) have been utilised to treat a wide variety of malignancies, including breast, ovarian, prostate, pancreatic, and lung [3]. Particularly, positive results obtained in studies with BRCA-mutant breast or ovarian cancer patients have made PARP inhibitors a standard treatment option [3].

Talazoparib is a potent PARP inhibitor, with both substantial catalytic inhibition and the capacity to induce PARP trapping at sites of DNA damage [4]. The EMBRACA trial was a randomized, phase 3 study and demonstrated the progression-free survival (PFS) benefit (HR:0.54) with talazoparib compared with single-agent therapy of the physician's choice in advanced hormone receptor-positive (HR+) or triple-negative breast cancer (TNBC) patients with BRCA1/2 mutation [5]. However, in contrast to other PARP inhibitors, there are very few data demonstrating talazoparib's efficacy in ovarian cancer [6]. Two phase 1 studies suggest it may have clinical benefits for the treatment of ovarian cancer patients [7, 8].

This study attempted to assess the efficacy of talazoparib in advanced breast and ovarian cancer patients with germline BRCA mutation. In addition to being a real-world analysis that included patients whose standard treatment choices had been exhausted for some, the objective of this study was to include a cohort of patients with ovarian cancer, a condition for which there were limited data on the efficacy of talazoparib.

Materials and methods

This multicenter, retrospective study enrolled advanced breast (HR + or TNBC) and ovarian cancer patients with BRCA1 and/or BRCA2 mutation. There were no exclusion criteria regarding treatment-line, metastatic sites or performance status. All patients received talazoparib treatment (1 mg, once daily) between September 2018 and May 2020 via early-access programme (EAP).

The study was conducted in 32 different centers in Turkey. Clinical and demographic characteristics, germline BRCA mutation analysis, pathology reports, and radiologic evaluations were obtained from patient files and hospital databases. Results were analysed separately for breast cancer (BC cohort) and ovarian cancer (OC cohort) patients. The end-points were the same for both cohorts.

The primary endpoint was PFS, which was defined as the period from the start of tazaloparib treatment to the disease progression or death. Secondary endpoints were overall survival (OS) and objective response rate (ORR). Overall survival was defined as the time from initiation of talazoparib to death from any cause. The ORR was defined as the percentage of patients who achieved a complete response (CR) or a partial response (PR) as determined by the investigator using RECIST version 1.1.

SPSS 22.0 was used for all statistical procedures (SPSS Inc, Chicago, Illinois). The Kaplan-Meier method was used to generate survival curves, and the log-rank test was used to compare survival differences. A statistically significant p-value of 0.05 was considered.

Results

The study population included 47 patients with advanced breast cancer and 42 patients with advanced ovarian cancer. Results were analysed and presented separately for each cohort.

Breast cancer cohort

There were 47 advanced breast cancer patients (46 female and one male). The median age of the group was 41.5. There were 59.6% of patients with HR(+) and 34% with TNBC. BRCA1 and BRCA2 mutations were seen in 42.6% ($n = 20$) and 48.9% ($n = 23$) of the patients, respectively. Four patients had BRCA mutation but the subtype did not specify and one patient had PALB2 mutation. There were only 2 patients who received talazoparib as first-line treatment and 48.9% of the patients ($n = 23$) received talazoparib treatment in the first 3-lines. The treatment-line varied from first to ninth. (Table 1)

The rate of the previous exposure to platinum compounds before talazoparib was 53.2% ($n = 25$). Twelve of these 25 patients had disease progression during treatment with platinum-based chemotherapy, which represents 25.5% of the study group. In the advanced setting of disease, the rate of patients who received chemotherapy

Table 1 Patient characteristics

Feature	BC Cohort ($n=47$)		OC Cohort ($n=42$)	
Age (median)	41.5 (26–69)		50 (34–66)	
Tumor Histology	HR (+)	59.6%, $n=28$	Serous	88%, $n=37$
	TNBC	34%, $n=16$	Clear cell	4.8%, $n=2$
	N/A	6.4%, $n=3$	N/A	4.8%, $n=2$
Disease stage at First Diagnosis	Stage II	36.2%, $n=17$	Stage I	4.8%, $n=2$
	Stage III	31.9%, $n=15$	Stage II	4.8%, $n=2$
	Stage IV	25.5%, $n=12$	Stage III	73.8%, $n=31$
	N/A	6.4%, $n=3$	Stage IV	14.3%, $n=6$
			N/A	2.4%, $n=1$
Metastatic Sites	Bone	57.4%, $n=27$	Periton and LN	80.9%, $n=34$
	Visceral	76.6%, $n=36$		33.3%, $n=14$
	CNS	12.8%, $n=6$	Visceral CNS	7.1%, $n=3$
Mutation Type	BRCA1	42.6%, $n=20$	BRCA1	52.4%, $n=22$
	BRCA2	48.9%, $n=23$	BRCA2	26.2%, $n=11$
	BRCA	6.3%, $n=3$	BRCA	21.4%, $n=9$
	PALB2	2.2%, $n=1$		
Treatment-Line of Talazoparib	1st	4.3%, $n=2$	1st	2.4%, $n=1$
	2nd	21.3%, $n=10$	2nd	16.7%, $n=7$
	3rd	23.4%, $n=11$	3rd	33.3%, $n=14$
	≥4th	51%, $n=24$	≥4th	47.6%, $n=20$

was 76.6% ($n=36$), 44.7% ($n=21$), 42.6% ($n=20$) and 21.3% ($n=10$) in the first, second, third and fourth-line respectively.

In this heavily pre-treated BC cohort, the ORR was 31.9% ($n=15$) and DCR was 61.7% ($n=29$). In 5 patients (10.6%) radiologically complete response (CR) was achieved with Talazoparib treatment (Table 2). The ORR of the subgroup which received the treatment in the first 3 lines was 34.7%. Among the patients who had previously progressed on platinum therapy, an objective response with talazoparib was observed in only two cases.

After median 13.6 months follow-up, there were 29 events and the median PFS for talazoparib treatment was 6.5 months (5.0–8.1 months, 95% CI) (Fig. 1A). The PFS between the patients whose BRCA1 ($n=18$) or BRCA2 ($n=21$) mutation was significantly differ (12.6 vs. 5.0 months, $p=0.005$). However, PFS difference according to treatment-line (≤3 or >3), age (<40 or ≥40) or sensitivity to previous platinum compounds was failed to reach statistical significance (Table 3). The median OS for Talazoparib treatment had not been reached but the estimated 12-month OS rate was 73.6%. (Fig. 1B) There was

Table 2 Response rates to Talazoparib treatment

Response	BC Cohort (%, *n*)	OC Cohort (%, *n*)
CR	10.6%, $n=5$	11.9%, $n=5$
PR	21.3%, $n=10$	35.7%, $n=15$
ORR	31.9%, $n=15$	47.6%, $n=20$
SD	29.8%, $n=14$	16.7%, $n=7$
PD	31.9%, $n=15$	26.2%, $n=11$
N/A	6.4%, $n=3$	9.5%, $n=4$

no difference in PFS between patients below and above 40 years of age.

At least one side effect reported in 61.7% of the patients and grade 3–4 toxicity was seen in 14 patients (29.8%). The most common side effect was hematologic cytotoxicity. Eleven patients (23.4%) experienced anemia and/or thrombocytopenia which required transfusion. The drug dose was reduced due to side effects in 15 patients (31.9%).

Ovarian cancer cohort

There were 42 advanced ovarian cancer patients in the study population. The median age of the group was 50. BRCA1 and BRCA2 mutations were seen in 52.4% ($n=22$) and 26.2% ($n=11$) of the patients, respectively. Most of the patients (88%, $n=37$) had serous carcinoma. There were 39 patients (90.4%) who received adjuvant platinum and taxane combination. In advanced disease setting, the treatment lines for talazoparib ranged from first to tenth (Table 1).

The rate of the previous exposure to platinum compounds before talazoparib treatment was 85.7%, 55%, and 25.8% in the first three lines, respectively. The progressive disease under platinum therapy was reported in 17 patients (40.5%).

The ORR was 47.6% ($n=20$) and DCR was 64.3% ($n=27$) with talazoparib. In 5 patients (11.9%) CR was achieved (Table 2).

After median 13.7 months follow-up, there were 25 events and the median PFS for talazoparib treatment was 9.1 months (7.3–10.8 months, 95% CI). (Fig. 2A). The median PFS was 10 months (7.9–12 months, 95% CI) and 5 months (0.9–9.2 months, 95% CI) for the platinum-sensitive ($n=24$) and -resistant ($n=17$) subgroups ($p=0.005$) (Table 3).

At the end of follow-up, 9 patients died and the median OS had not been reached. The estimated 12-month OS rate was 75.9%. (Fig. 2B)

At least one side effect reported in 59.5% of the patients and grade 3–4 toxicity was seen in 15 patients (35.7%). The most common side effect was hematologic cytotoxicity. 16 patients (38.1%) experienced anemia and/or thrombocytopenia which required transfusion. The drug dose was reduced due to side effects in 12 patients (28.6%). During the follow-up period, no cases of acute myeloid leukemia or myelodysplastic syndrome were observed.

Discussion

In our study, we assessed the efficacy of talazoparib therapy in patients with advanced germline BRCA-mutant breast and ovarian cancer who had received extensive prior treatment. The primary endpoint PFS was 6.5 and 9.1 months, the secondary endpoint OS was 73.6% and

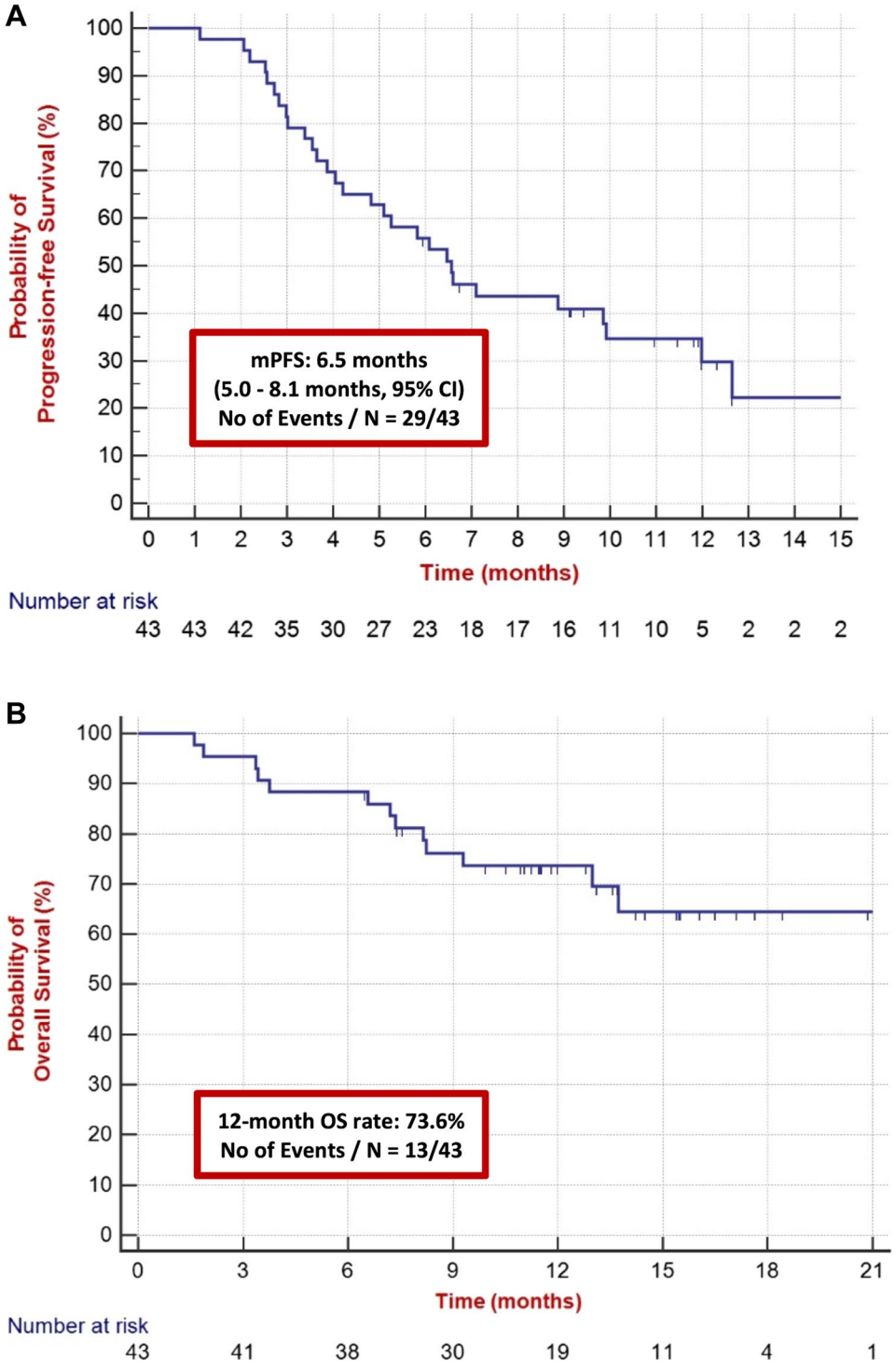

Fig. 1 **A** Progression-free Survival for Breast Cancer Cohort. **B** Overall Survival for Breast Cancer Cohort

75.9% at 12 months, and the ORR was 31.9% and 47.9%, in the BC and OC cohorts, respectively. Consistent with the study design, cohorts were discussed separately.

The EMBRACA phase 3 study demonstrated the efficacy of talazoparib in patients with advanced HR(+) or triple-negative breast cancer [5]. In this trial, the median age of the 287 patients assigned to the talazoparib arm was 45 years, 54.7% had HR+, and 69.7% had visceral disease. Despite the modest size of our BC cohort, the median age (41.5) and HR + disease rate (59.6%) were comparable to the phase 3 pivotal research. In our analysis, the prevalence of visceral metastases was slightly

Table 3 Progression-free survival in subgroups

BC Cohort			
Subgroup	**No. of Event/N**	**PFS (median, 95% CI)**	***P***
Treatment-Line	11/20	9.9 months (4.3–15.4)	0.053
≤ 3rd	18/23	3.8 months (1.4–6.2)	
≥ 4th			
Mutation	9/18	12.6 months (8.6–16.6)	0.005
BRCA1	17/21	5.0 months (2.6–7.5)	
BRCA2			
Histology	17/26	6.4 months (4.7–8.1)	0.87
HR (+)	12/16	6.0 months (NE – 13.2)	
TNBC			
Previous Platinum	16/25	8.8 months (1.8–15.9)	0.71
Yes	7/12	6.6 months (3.9–9.2)	
No			
OC Cohort			
Subgroup	**No. of Event/N**	**PFS (median)**	***P***
Treatment-Line	10/22	10.6 months (8.1–13.1)	0.10
≤ 3rd	15/20	7.8 months (1.5–14.0)	
≥ 4th			
Mutation	14/22	5.7 months (0.5–10.9)	0.21
BRCA1	5/11	11.2 months (9.1–13.2)	
BRCA2			
Platinum-Sensitive	11/24	10.0 months (7.9–12.0)	0.005
Resistant	14/17	5.0 months (0.9–9.2)	

(76.6%) higher. Again, the rates of being BRCA1- or BRCA2-positivity (about 50%) are comparable [5]. In large-scale studies conducted in Turkey on the distribution of BRCA mutations, BRCA2 has been reported to occur more frequently, especially among breast cancer patients [9, 10].

In the pivotal phase 3 study, the median PFS for the talazoparib arm was 8.6 months [5]. Our finding reveals this value to be 6.5 months. As is typical in research reporting real-world data, it is possible to claim that patients' performance and comorbidities may be worse than in clinical trials. However, while the median PFS value of 6.5 months makes sense, the fact that the BC cohort's patients were extensively pretreated was clearly the most relevant factor. In contrast to the phase 3 study in which patients who received more than three prior cytotoxic regimens were excluded and 38.7% of patients did not receive any cytotoxic therapy, more than half of the patients in our cohort had access to talazoparib at fourth line and beyond [5]. Although it failed to reach statistical significance (p = 0.053), the dramatic difference between 9.9 and 3.8 months PFS obtained in patients who received talazoparib in the first three-lines compared to those who received in subsequent lines supported this idea.

One of the secondary outcomes, ORR was 31.9% in the BC cohort. In light of the 62.6% ORR revealed in the phase 3 study, it can be stated that it falls below expectations. As with PFS, it is critical that patients be extensively pretreated when examining ORR outcomes [5]. ABRAZO was another research investigating the efficacy of talazoparib in advanced breast cancer patients with BRCA mutations [11]. This was a phase 2 trial with two cohorts and an open-label design. Cohort 1 was comprised of patients who responded to prior platinum with no progression within 8 weeks of the last dose, and cohort 2 was comprised of patients who had at least three platinum-free cytotoxic regimens for advanced breast cancer. In these two cohorts, the reported ORR was 21% and 37%, respectively [11]. A 31.9% ORR was acceptable given that almost half of our study population had platinum exposure, a quarter of them progressed under platinum treatment, and approximately half of them had previously received three-lines of treatment.

A significant difference in PFS observed between patients with BRCA1 and BRCA2 mutations, in favor of patients with BRCA1 mutations. There was no conclusion in the subgroup analysis of prospective phase studies of talazoparib or other PARP inhibitors that might explain this discrepancy. Moreover, a 2021 meta-analysis involving 11 distinct phase studies (6 ovarian, 3 breast, 1 prostate, and 1 pancreatic cancer) in which PARP inhibitors (olaparip, rucaparib, talazoparib, veliparib, niraparib) were tested revealed that there was no difference in efficacy between BRCA1 and BRCA2 mutations [12]. The PFS difference in our study could be explained by the nature of the retrospective studies in which patients were not stratified, as well as the small number of patients.

Patients in the control arm of the EMBRACA trial (as in the OlympiAD study in which olaparib was examined) were given chemotherapy of the investigator's choice, although platinum was not permitted. Nevertheless, there was no significant difference in OS favoring talazoparib in the 2020 update of the trial. The median OS was reported 19.3 months and the 1-year survival was 71% with talazoparib [13, 14]. The short follow-up period is one of the limitations of our research, but the 1-year OS obtained in our study, at 73.6%, is very similar to this level, despite the fact that the patient group was treated more aggressively and for a longer period of time.

To the best of our knowledge, our study includes the largest cohort of ovarian cancer patients treated with talazoparib. There is no phase 3 trial evaluating talazoparib's efficacy in ovarian cancer and the drug is not approved for daily clinical practice. Two phase 2 clinical trials were early terminated and withdrawn [6]. The impact of the discussion may be limited by the lack of prospective data, but this limitation emphasizes that our study, with its cohort of 42 ovarian cancer patients, made a substantial contribution to the literature.

34 ovarian cancer patients were participated in the phase 1 study of talazoparib. Although the primary objective of the phase 1 study was not to evaluate efficacy, in 12 BRCA-mutant patients with measurable disease who

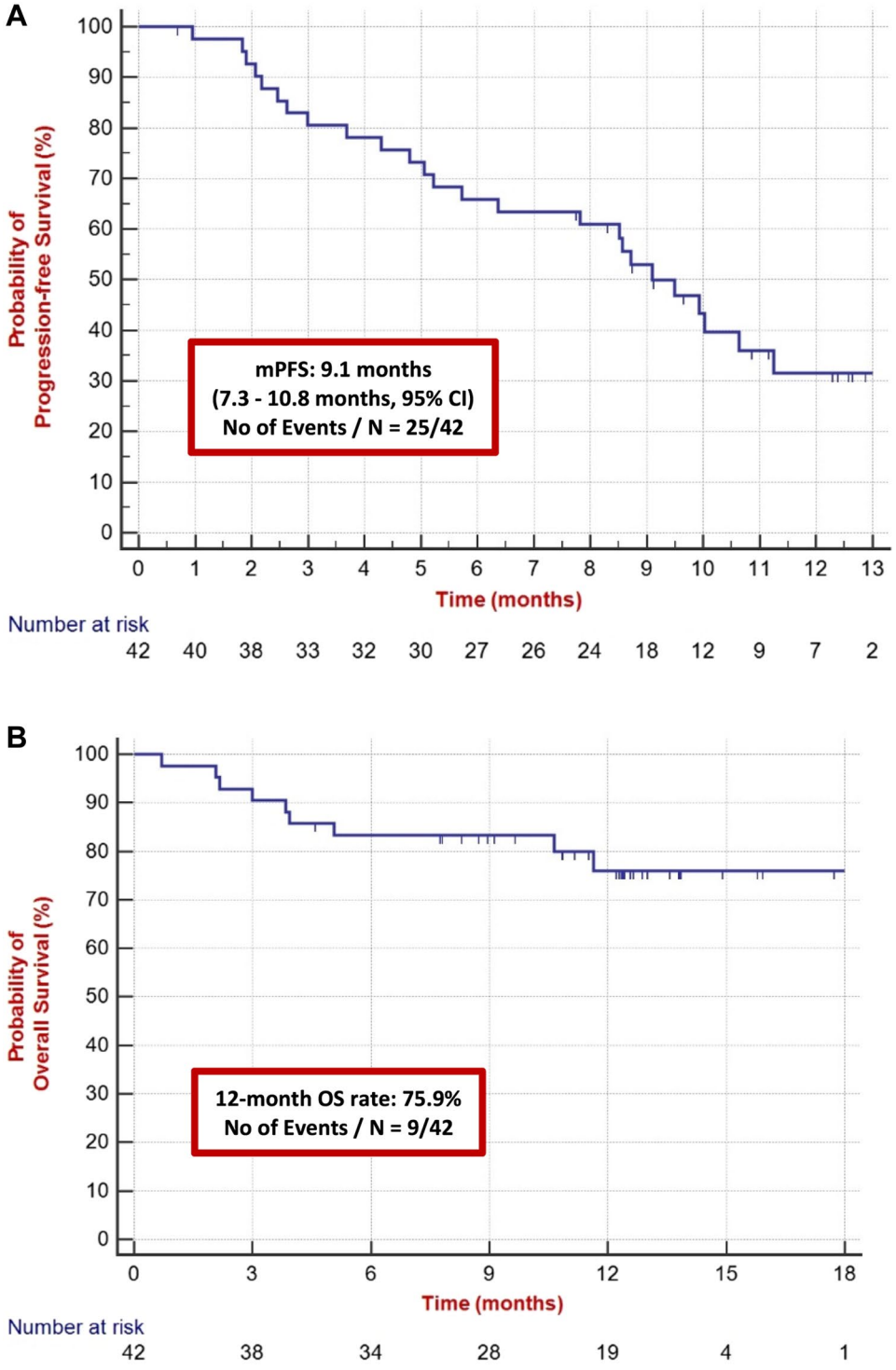

Fig. 2 **A** Progression-free Survival for Ovarian Cancer Cohort. **B** Overall Survival for Ovarian Cancer Cohort

were treated with 1.0 mg/day, the ORR and clinical benefit rate (CBR) lasting at least 24 weeks were 42% and 67%, respectively, with a median PFS of 36.4 weeks [7]. In our study, the median PFS was 9.1 months, and given that 80% of the patients had previously received at least three stages of cytotoxic therapy, this result may not have been below expectations.

In our study, platinum-sensitive patients (57.1%) had a much longer median PFS than platinum-resistant (40.4%) patients (10 vs. 5 months). Particularly based on olaparib research findings, it is acknowledged that PARP

inhibitors have limited efficacy in platinum-resistant disease. In one of these investigations, the mPFS was reported as 7 months for 193 patients with platinum-resistant ovarian cancer who received an average of 4.3 treatment lines [15]. Another real-world data analysis with 28 patients (5 of whom received talazoparib) found that the median PFS in platinum-sensitive patients (n = 11) was roughly twice that of platinum-resistant patients (n = 17) (16.6 vs. 8.4 months, p = 0.013), which is consistent with our findings [16].

The ORR was 47.6%. Similar to our cohort, another research including olaparib revealed an ORR of 46% in platinum-sensitive and 30% in platinum-resistant patients who had received at least three lines of chemotherapy [17]. In the olaparib study, the extensively pretreated BRCA-mutant ovarian cancer cohort had a median OS of 16.6 months, and the 1-year OS rate of 75.9% appeared consistent with the literature, despite the short follow-up period [15].

As a classic example of a multicenter retrospective study, our study had several flaws, including patient selection bias, differences between centers, a lack of radiological central evaluation, a small number of patients, and high-level heterogeneity.

Another critical fact is that no PARP inhibitors were available in our country. Oncologists hope to make early access programs, which can only be applied for a limited time, available to their patients, many of whom have exhausted their conventional therapy options. This characteristic may have generated a situation that was completely contradictory to the patient selection criteria for phase trials, resulting in a highly heterogeneous patient cohort. Despite its limitations, the outcome of OC cohort contributes to the literature on PARP inhibitors in BRCA mutant ovarian cancer.

Authors' contributions

MANS and MH are co-first author of this paper. MANS and MH researched literature and conceived the study. MANS was involved in protocol development, gaining ethical approval, patient recruitment and data analysis. MH wrote the first draft of the manuscript. All authors contributed study design, ethical approval, patient recruitment and data collection. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

Funding

No role for any funding source.

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request. All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki, and approval was obtained (No: E2-20-127, 30-Dec-2020) from the Ethics Committee of the Ankara City Hospital. The requirement for written informed consent was waived by the Ethics Committee of the Ankara City Hospital due to the retrospective nature of the study.

Conflict of interest

The authors declare no conflicts of interest.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Medical Oncology, Faculty of Medicine, Ankara Yıldırım Beyazıt University, Ankara, Turkey
[2]Department of Medical Oncology, Ankara Bilkent City Hospital, 1604. Cadde, No: 9, Ankara, Turkey
[3]Department of Medical Oncology, Faculty of Medicine, Ege University, İzmir, Turkey
[4]Department of Medical Oncology, Faculty of Medicine, Dokuz Eylul University, İzmir, Turkey
[5]Department of Medical Oncology, Ankara Abdurrahman Yurtaslan Oncology Training and Research Hospital, Ankara, Turkey
[6]Department of Medical Oncology, Hacettepe University Cancer Institute, Ankara, Turkey
[7]Department of Medical Oncology, Gulhane Education and Research Hospital, Ankara, Turkey
[8]Department of Medical Oncology, Faculty of Medicine, Cukurova University, Adana, Turkey
[9]Department of Medical Oncology, Faculty of Medicine, Pamukkale University, Denizli, Turkey
[10]Department of Medical Oncology, Kayseri Acıbadem Hospital, Kayseri, Turkey
[11]Department of Medical Oncology, Medicana International Hospital, İzmir, Turkey
[12]Department of Medical Oncology, Istanbul University Institute of Oncology, İstanbul, Turkey
[13]Department of Medical Oncology, Faculty of Medicine, Erciyes University, Kayseri, Turkey
[14]Department of Medical Oncology, Gaziantep Medical Point Hospital, Gaziantep, Turkey
[15]Department of Medical Oncology, Faculty of Medicine, Gazi University, Ankara, Turkey
[16]Department of Medical Oncology, Acıbadem Adana Hospital, Adana, Turkey
[17]Department of Medical Oncology, Bakırköy Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[18]Department of Medical Oncology, Faculty of Medicine, Meram University, Konya, Turkey
[19]Department of Medical Oncology, Faculty of Medicine, Bezmialem Vakif University, İstanbul, Turkey
[20]Department of Medical Oncology, Manisa City Hospital, Manisa, Turkey
[21]Department of Medical Oncology, Faculty of Medicine, Akdeniz University, Antalya, Turkey
[22]Department of Medical Oncology, Faculty of Medicine, Baskent University, Adana, Turkey
[23]Department of Medical Oncology, Health Science University Medical Faculty, Prof Dr Cemil Taşçioğlu City Hospital, Istanbul, Turkey
[24]Department of Medical Oncology, Medical Park Florya Hospital, Istanbul, Turkey
[25]Department of Medical Oncology, Faculty of Medicine, Acıbadem University, İstanbul, Turkey
[26]Department of Medical Oncology, Avrasya Hospital, İstanbul, Turkey
[27]Department of Medical Oncology, Faculty of Medicine, Cerrahpasa University, İstanbul, Turkey
[28]Department of Medical Oncology, Faculty of Medicine, Medipol University, Istanbul, Turkey
[29]Department of Medical Oncology, Memorial Ankara Hospital, Ankara, Turkey
[30]Department of Medical Oncology, Faculty of Medicine, Istinye University, Istanbul, Turkey
[31]Department of Medical Oncology, Faculty of Medicine, Celal Bayar University, Manisa, Turkey
[32]Department of Medical Oncology, Faculty of Medicine, Medeniyet University, Istanbul, Turkey

[33]Department of Medical Oncology, Acıbadem Atakent Hospital, Istanbul, Turkey
[34]Department of Medical Oncology, Memorial Bahcelievler Hospital, İstanbul, Turkey

Received: 15 August 2024 / Accepted: 2 November 2025
Published online: 22 November 2025

References

1. Rose M, Burgess JT, O'Byrne K, Richard DJ, Bolderson E. PARP inhibitors: clinical relevance, mechanisms of action and tumor resistance. Front Cell Dev Biol. 2020. https://doi.org/10.3389/fcell.2020.564601.
2. Gorodetska I, Kozeretska I, Dubrovska A. BRCA, genes. The role in genome stability, cancer stemness and therapy resistance. J Cancer. 2019;10(9):2109–27.
3. Schettini F, Giudici F, Bernocchi O, Sirico M, Corona SP, Giuliano M, et al. Poly (ADP-ribose) polymerase inhibitors in solid tumours: systematic review and meta-analysis. Eur J Cancer. 2021;149:134–52.
4. Shen Y, Rehman FL, Feng Y, Boshuizen J, Bajrami I, Elliott R, et al. BMN 673, a novel and highly potent PARP1/2 inhibitor for the treatment of human cancers with DNA repair deficiency. Clin Cancer Res. 2013;19(18):5003–15.
5. Litton JK, Rugo HS, Ettl J, Hurvitz SA, Gonçalves A, Lee K-H, et al. Talazoparib in patients with advanced breast cancer and a germline *BRCA* mutation. N Engl J Med. 2018;379(8):753–63.
6. Boussios S, Abson C, Moschetta M, Rassy E, Karathanasi A, Bhat T, et al. Poly (ADP-ribose) polymerase inhibitors: talazoparib in ovarian cancer and beyond. Drugs RD. 2020;20(2):55–73.
7. de Bono J, Ramanathan RK, Mina L, Chugh R, Glaspy J, Rafii S. Phase I, dose-escalation, two-part trial of the PARP inhibitor talazoparib in patients with advanced germline BRCA1/2 mutations and selected sporadic cancers. Cancer Discov. 2017;7(6):620–9.
8. Dhawan MS, Bartelink IH, Aggarwal RR, Leng J, Zhang JZ, Pawlowska N, et al. Differential toxicity in patients with and without DNA repair mutations: phase I study of carboplatin and Talazoparib in advanced solid tumors. Clin Cancer Res. 2017;23(21):6400–10.
9. Bisgin A, Sag SO, Dogan ME, Yildirim MS, Gumus AA, Akkus N, et al. Germline landscape of BRCAs by 7-site collaborations as a BRCA consortium in Turkey. Breast. 2022;65:15–22.
10. Boga I, Ozemri Sag S, Duman N, Ozdemir SY, Ergoren MC, Dalci K, et al. A multicenter study of genotype variation/demographic patterns in 2475 individuals including 1444 cases with breast cancer in Turkey. Eur J Breast Health. 2023;19(3):235–52.
11. Turner NC, Telli ML, Rugo HS, Mailliez A, Ettl J, Grischke EM, et al. A phase II study of Talazoparib after platinum or cytotoxic nonplatinum regimens in patients with advanced breast cancer and germline BRCA1/2 mutations (ABRAZO). Clin Cancer Res. 2019;25(9):2717–24.
12. Li S, Tao L, Dai H, Gong X, Zhuo Y, Xiang H, et al. BRCA1 versus BRCA2 and PARP inhibitors efficacy in solid tumors: a meta-analysis of randomized controlled trials. Front Oncol. 2021;11:718871.
13. Litton JK, Hurvitz SA, Mina LA, Rugo HS, Lee KH, Goncalves A, et al. Talazoparib versus chemotherapy in patients with germline BRCA1/2-mutated HER2-negative advanced breast cancer: final overall survival results from the EMBRACA trial. Ann Oncol. 2020;31(11):1526–35.
14. 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;377(6):523–33.
15. Kaufman B, Shapira-Frommer R, Schmutzler RK, Audeh MW, Friedlander M, Balmana J, et al. Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation. J Clin Oncol. 2015;33(3):244–50.
16. Agarwal A, Baghmar S, Dodagoudar C, Qureshi S, Khurana A, Vaibhav V, et al. PARP inhibitor in platinum-resistant ovarian cancer: single-center real-world experience. JCO Glob Oncol. 2021;7:506–11.
17. Domchek SM, Aghajanian C, Shapira-Frommer R, Schmutzler RK, Audeh MW, Friedlander M, et al. Efficacy and safety of Olaparib monotherapy in germline BRCA1/2 mutation carriers with advanced ovarian cancer and three or more lines of prior therapy. Gynecol Oncol. 2016;140(2):199–203.

Publisher's Note