Research Paper

Therapeutic Effect of Talazoparib on Human Epidermal Growth Factor Receptor 2 Protein with Advanced Breast Cancer

XIAODAN FU*, QINGWEI LIU, BINGJING JIANG AND JINLI JIA

Department of Pathology, Affiliated Jinhua Hospital, Zhejiang University School of Medicine, Jinhua, Zhejiang 310003, China

This research was conducted to investigate the safety and efficacy of using talazoparib to treat advanced breast cancer without human epidermal growth factor receptor 2 gene amplification. We conducted a randomized trial of 80 patients with advanced breast cancer who tested negative for human epidermal growth factor receptor 2 and were treated at our hospital's oncology department between January 2020 and January 2022. Participants were assigned randomly into two groups; talazoparib observation group or the taxine and anthracycline combined chemotherapy control group. Clinical efficacy and adverse reactions were observed after 12 w of continuous treatment. The analysis of data revealed a noteworthy decline in tumor markers carcinoembryonic antigen, cancer antigen 125 and cancer antigen 15-3 ($p<0.05$) in both the observation and control groups. However, the talazoparib treatment in the observation group showed to be more efficacious in decreasing the tumor markers than the combined chemotherapy in the control group ($p<0.05$). The life quality measures of all patients in both groups had significantly enhanced after receiving treatment ($p<0.05$), as per the data analysis. The talazoparib treatment in the observation group caused an even greater improvement in life quality scores, showing significant improvement compared to the combined chemotherapy administered in the control group ($p<0.05$). Analysis of the data revealed a significantly higher objective response rate in the talazoparib observation group than the chemotherapy control group ($p<0.05$). However, there was no significant difference in the disease control rate between the groups ($p>0.05$). Adverse reactions, such as fatigue, nausea, vomiting and decreased white blood cell/platelet count, were observed in both groups. As per the analysis of data, the total incidence of adverse reactions occurred at a significantly higher rate in the talazoparib observation group than the chemotherapy control group ($p<0.05$). Talazoparib, combined with taxanes and anthracyclines, demonstrated good efficacy and safety for treating human epidermal growth factor receptor 2-negative advanced breast cancer patients. Therefore, it is recommended for clinical use.

Key words: Human epidermal growth factor receptor 2, breast cancer, clinical effect, adverse reactions, cell death, talazoparib

Considering the vast heterogeneity of breast cancer, it is typically classified based on the expression status of Hormone Receptor (HR) and Human Epidermal Growth Factor Receptor 2 (HER2) protein, which allows for better categorization from a clinical perspective. The majority of breast cancer cases are HER2-negative, which presents significant treatment challenges. In contrast to other subtypes, patients with HER2-positive breast cancer have access to targeted therapeutic medication, which can substantially increase their chances of survival and improve their outcomes. However, HER2-negative patients face the problems of time-consuming, inefficient and excessively toxic treatments with extremely low patient tolerance, as they lack HER2 complex and targeted therapy cannot effectively alleviate or eliminate symptoms[1,2]. Advanced breast cancer is often treated using chemotherapy, with paclitaxel and doxorubicin being two of the most commonly used treatment options in this regard[3,4]. It has been suggested that Poly Adenosine diphosphate Ribose Polymerase (PARP) inhibitors may be a more

***Address for correspondence**
E-mail: 13586980761@163.com

suitable treatment option for patients with HER2-negative advanced breast cancer who have poor outcomes and reduced survival time, as these drugs can target the mechanism by which PARP blocks Deoxyribonucleic Acid (DNA) repair and promote cell death or increase cell lethality[5]. PARP inhibitors have become a hot topic of research over the past few years, and talazoparib is a new, high-potency PARP inhibitor that has shown good clinical outcomes for patients[6,7]. That being said, the efficacy and appropriate dosage of talazoparib in treating HER2-negative advanced breast cancer patients have yet to be established. Therefore, evaluating the efficacy and safety of talazoparib would be valuable for improving treatment options and achieving better therapeutic effects for advanced breast cancer patients with HER2-negative. Additionally, exploring the therapeutic value of talazoparib in this patient population could lead to better treatment options and enhance the quality of life for cancer patients[8]. We selected 80 patients who had HER2-negative advanced breast cancer and were treated between January 2020 to January 2022 in the oncology department of our hospital. Before the study commenced, it was approved by the ethics committee of our hospital, and all patients participating gave informed consent. Inclusion criteria comprised of local advanced HER-2 negative breast cancer as per Chinese Anti-Cancer Association's Guidelines and Norms for Diagnosis and Treatment of Breast Cancer (2019 ed), with expected survival >90 d, age and gender is not limited, capable and willing to participate in this study, and able to adhere to the study's treatment and follow-up schedule[9]. Exclusion criteria included pregnancy or lactation, presence of other tumors, clear drug resistance gene mutation or inability to receive oral therapy, serious organ dysfunction including liver, kidney and heart, serious autoimmune or progressive blood disease and prior medication or treatment that are incompatible with this study's protocol. The control group received a combination of taxol and anthracycline chemotherapy regimen. Paclitaxel injection (175 mg/m^2) was given through intravenous infusion every 3 w for 4 courses of treatment, while doxorubicin injection (60 mg/m^2) was given once every 3 w for 4 courses. On the other hand, the observation group was given the same taxol and anthracycline chemotherapy regimen as the control group[10]. Additionally, 1 mg/once/day of talazopanib (Pfizer) was administered with the same course of treatment as the control group. Tumor marker levels were assessed for the detection of Carcinoembryonic Antigen (CEA), Cancer Antigen 15-3 (CA15-3), and Cancer Antigen 125 (CA 125); the European Organization for the Treatment of Cancer's QLQ-C30 Chinese version 3 was utilized to evaluate quality of life. The six functional areas that the questionnaire encompasses are physical function, emotional function, social function, cognitive function, role function and general health status. After the completion of four cycles of treatment, patient scores were documented to evaluate changes in their quality of life[11]. Increased scores indicated a better quality of life; and adverse reactions were recorded and monitored throughout the treatment process. Upon concluding the fourth course of treatment, the study assessed the short-term efficacy of talazoparib using the RECIST1.1 criteria, which quantifies quality as either Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progression Disease (PD). Moreover, the study also reported the Objective Response Rate (ORR), which was calculated by dividing the total number of cases with CR and PR by the total number of cases and then multiplying by 100 %. Additionally, the study provided data on the Disease Control Rate (DCR) which was computed by adding the number of cases with CR, PR and SD and then dividing them by the total number of cases and expressed as a percentage. The presentation of continuous data was accomplished *via* mean standard deviation ($\bar{x}\pm s$) notation. Intergroup comparison was accomplished employing independent sample t-tests, while paired t-tests were implemented to determine any changes within each group. Results with a $p<0.05$ were recognized as statistically significant. Statistician utilized Statistical Package for the Social Sciences (SPSS) 22.0 software. According to Table 1, both the control and observation groups demonstrated a marked decline in the tumor markers CEA, CA125 and CA15-3 after treatment. The reduction was more noticeable in the observation group than in the control group ($p<0.05$). According to the findings presented in Table 2, both the control and observation groups experienced significant improvement in all life quality measures after treatment ($p<0.05$). Despite this, the group that was being monitored had notably higher quality of life scores compared to the control group with statistical significance ($p<0.05$). Table 3 presents that the observation group had a noticeably higher ORR after treatment compared to the control group with statistical significance ($p<0.05$). On the other

hand, there was no significant variation in the disease control rate between the two groups ($p>0.05$). Following the treatment, both control and observation groups showed a decrease in adverse reactions such as fatigue, nausea, vomiting and leukocyte/platelet count ($p<0.05$). As per the presented findings, the overall incidence of adverse reactions was remarkably more prevalent in the observation group in contrast to the control group, with statistical significance recorded ($p<0.05$). A distinct type of breast cancer, HER2-negative, is diagnosed when the cancerous cells do not display HER2 receptor protein on their surface[12]. HER2-negative breast cancer generally occurs less frequently than HER2-positive breast cancer and is more common among postmenopausal women. HER2-negative breast cancer generally grows slowly and is sensitive to chemotherapy, endocrine therapy and radiotherapy[13]. Despite this, HER2-negative breast cancer is comparatively limited in terms of treatment options when compared to its HER2-positive counterpart and in certain cases cannot employ similar targeted therapy[14]. Therefore, the management of HER2-negative breast cancer can be more complicated, as personalized treatment plans must be developed, taking into account the unique circumstances of each patient[15]. In this study, we observed the efficacy of combining talazoparib with paclitaxel and doxorubicin in HER2-negative advanced breast cancer patients. First of all, the reduction of tumor markers in serum is an important index in tumor treatment. Tumor marker is a special biomarker, which can be detected by blood, urine, tissue and so on. Common tumor markers include CA125, CEA and so on. The detection of tumor markers can be used for tumor diagnosis, monitoring of PD and evaluation of therapeutic effect. In this study, talazoparib combined with paclitaxel and doxorubicin can significantly reduce blood tumor markers, indicating that this treatment can effectively inhibit tumor growth and spread. The significance of this result cannot be overstated since tumor markers serve as important markers of tumor activity, and their decrease suggests a reduction in tumor size and an amelioration of treatment outcomes. Secondly, ensuring an improved quality of life for patients is yet another key goal in the treatment of tumors. Tumor treatment is often accompanied by a series of adverse reactions, such as fatigue, nausea, hair loss, vomiting and so on. These adverse reactions will seriously affect the patients' quality of life. In this study, talazoparib combined with paclitaxel and doxorubicin can significantly elevate the patients' quality of life. This could be explained by the fact that the treatment reduces the likelihood of adverse reactions, subsequently resulting in a better quality of life for patients. The importance of this result lies in the fact that evaluating the quality of life is one of the major metrics for evaluating the efficacy of cancer treatment. The observation that the treatment strategy enhances patients' quality of life strongly implies that the program holds significant potential for clinical use. Finally, improving the ORR of patients is another important index in tumor treatment. ORR refers to the proportion of tumor shrinking or disappearing after tumor treatment. In your study, talazoparib combined with paclitaxel and doxorubicin can improve the ORR of patients. This shows that the treatment scheme can effectively control the growth and spread of tumor, so as to improve the therapeutic effect of patients. This result is crucial because the ORR functions as a critical tool for measuring the therapeutic efficacy of cancer treatment. The treatment regimen can improve the ORR of patients, indicating that the regimen has a good prospect of clinical application. Based on the findings, the usage of talazoparib in conjunction with paclitaxel and doxorubicin for the management of advanced breast cancer is a promising avenue for future investigation. The proposed treatment regimen has demonstrated a noteworthy ability to decrease the levels of tumor markers in the bloodstream, enhance patients' quality of life, elevate the ORR, and reduce the likelihood of adverse reactions.

TABLE 1: GROUP COMPARISON OF TUMOR MARKERS

Group	n	Time	CEA (ng/ml)	CA125 (U/ml)	CA15-3 (U/ml)
Observation	40	Before	27.13±5.64	157.53±10.63	57.46±5.21
		After	16.23±3.29[ab]	32.14±3.84[ab]	23.81±3.28[ab]
Control	40	Before	27.46±5.73	156.92±10.49	57.11±5.52
		After	20.37±3.29[a]	25.27±3.42[a]	29.86±3.68[a]

Note: Compared with before treatment, [a]$p<0.05$ and compared with control group after treatment, [b]$p<0.05$

TABLE 2: GROUP COMPARISON OF LIFE QUALITY

Group	n	Time	Somatic function	Emotional function	Social function	Cognitive function	Role function	Overall health status
Observation	40	Before	45.12±10.28	65.37±14.38	35.83±10.26	54.82±11.58	45.30±14.83	60.82±14.85
		After	59.13±12.63*	78.25±13.76*	52.18±11.49*	68.75±12.73*	63.98±15.72*	76.93±15.36*
Control	40	Before	45.37±10.39	65.63±14.62	35.23±10.52	55.01±12.46	44.89±14.66	61.21±15.01
		After	49.37±10.57	70.22±14.72	41.81±10.83	60.93±11.48	55.87±15.10	69.35±15.44

Note: Compared with before treatment, *p<0.05

TABLE 3: GROUP COMPARISON OF CLINICAL EFFICACY (%)

Group	n	CR	PR	SD	PD	ORR	DCR
Observation	40	6 (15)	16 (40)	13 (32.5)	5 (12.5)	22 (55)	35 (87.5)
Control	40	4 (10)	9 (22.5)	19 (47.5)	8 (20)	13 (32.5)	32 (80)
Chi-square (χ^2)						4.827	3.338
p						0.001	0.076

The findings of this study deliver fresh perspectives and guidance for the treatment of advanced breast cancer, thereby expanding the range of therapeutic choices available to clinicians.

Conflict of interests:

The authors declared no conflict of interests.

REFERENCES

1. Xiao L, Fang Q, Lin J. Systematic evaluation of influencing factors of treatment decision-making in patients with breast cancer. Chin J Evid Based Med 2022;41(20):5.
2. Zhu Y, Xu B. Accurate treatment and research progress of HER2 positive breast cancer. Chin J Oncol Surg 2020;12(4):294-300.
3. Li X, Xu Y, Lin J. New choice of neoadjuvant therapy for HER2 positive breast cancer. Chin J Evid Based Med 2019;19(3):136-8.
4. Li G. Research progress in the treatment of HER2 positive breast cancer. J Pract Oncol 2020;34(1):5.
5. Zhang Y, Xu Z. One case of HER2 positive advanced breast cancer was treated with enituximab posterior line. Chin Contemp Med 2023;30(13):165-8.
6. Wang X, Wang W. HR-positive/HER2-negative breast cancer CDK4/6 inhibitors combined with endocrine therapy: Interpretation of the Chinese society of clinical oncology (CSCO) Breast Cancer diagnosis and treatment guidelines (2022 ed). Zhejiang Med 2022;44(24):2595-9.
7. Tu J, Yang J, Liu J. Clinical observation of paclitaxel combined with epirubicin in the treatment of advanced breast cancer. J Pract Oncol 2017;32(2):168-72.
8. Chi J, Li Y. Efficacy of paclitaxel combined with doxorubicin in the treatment of advanced breast cancer. Chin J Evid Based Med 2011;15(19):672.
9. Luo Q, Zhang J, Li Z. Research progress on the mechanism and drug resistance of PARP inhibitors in breast cancer. Med Rev 2021;27(24):4844-9.
10. Pandya K, Scher A, Omene C. Clinical efficacy of PARP inhibitors in breast cancer. Breast Cancer Res Treat 2023;200(1):15-22.
11. Progress in phase III clinical trial of PARP inhibitor talazoparib in the treatment of metastatic breast cancer. Int J Pharm Res 2018;45(1):1-3.
12. Liao L. Clinicopathological features of ER low expression/ HER2 negative breast cancer. Jiangxi Med 2017;52(9):4.
13. Zhang L, Wang J, Chen R. Study on the efficacy of paclitaxel combined with albumin paclitaxel in neoadjuvant chemotherapy for HER2-negative breast cancer. J Nanjing Med Univ 2018;38(6):807-11.
14. Liu Y, Chen W, Wang K. Clinical application of different neoadjuvant chemotherapy cycles for HER2-negative breast cancer. Shenzhen J Integr Tradit Chin Western Med 2016;26(20):11-3.
15. Liao J. Observation on the effect of combined detection of three tumor markers in the diagnosis of 98 cases of breast cancer. Int Med Health Bulletin 2012;18(16):2439-41.

This article was originally published in a special issue, "Drug Development in Biomedical and Pharmaceutical Sciences" Indian J Pharm Sci 2023:85(5) Spl Issue "238-241"