Breast Cancer: Targets and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Prognostic Significance of Pretreatment Mean Platelet Volume in Patients with Recurrent or De Novo Metastatic Breast Cancer: A Single-Center Retrospective Study

Zeynep Sıla Gökdere[1], Damla Günenç[2], Serdar Sezer[3], Aslı Geçgel[4], Filiz Çay Şenler[5]

[1]Ege University Faculty of Medicine, Department of Medical Oncology, Izmir, 35100, Türkiye; [2]Izmir Training and Research Hospital, Department of Medical Oncology, İzmir, 35100, Türkiye; [3]Ankara University Faculty of Medicine, Department of Rheumatology, Ankara, 06230, Türkiye; [4]Kartal Dr. Lütfi Kırdar Training and Research Hospital, Department of Medical Oncology, İstanbul, 34865, Türkiye; [5]Ankara University Faculty of Medicine, Department of Medical Oncology, Ankara, 06620, Türkiye

Correspondence: Zeynep Sıla Gökdere, Department of Medical Oncology Kazımdirik, Université Avenue (Cd.) No:9, Ege University Faculty of Medicine, İzmir, 35100, Türkiye, Email silagokdere@hotmail.com

Breast Cancer: Targets and Therapy downloaded from https://www.dovepress.com/
For personal use only.

Background: Breast cancer is the most prevalent malignancy among womificant advances in systemic therapies, metastatic breast cancer remains largely incurable, highlighting the need for reliable prognostic biomarkers. Mean platelet volume (MPV), a routinely measured hematological parameter reflecting platelet size, has been linked to platelet activation, systemic inflammation, and tumor progression. However, the prognostic significance of MPV in recurrent or de novo metastatic breast cancer is unclear. This study evaluated the association between pretreatment MPV and overall survival in this patient population.

Methods: A retrospective analysis was conducted on 200 women with recurrent or de novo metastatic breast cancer. Clinical, pathological, and hematological data were collected from medical records. Pretreatment MPV was measured prior to initiation of systemic therapy. MPV was assessed using both the institutional laboratory upper reference limit of 10.5 fL and an exploratory receiver operating characteristic-derived cutoff of 9.55 fL. Overall survival was defined as the interval from diagnosis of recurrent or de novo metastatic disease to death from any cause or last follow-up. Survival outcomes were compared according to MPV status.

Results: Pretreatment MPV was not significantly associated with overall survival in patients with recurrent or de novo metastatic breast cancer. Using the institutional cutoff of 10.5 fL, median overall survival was 48 months for patients with MPV <10.5 fL (95% CI: 38.161–57.839) and 108 months for those with MPV ≥10.5 fL (95% CI: 26.214–189.800), with no statistically significant difference between groups (p = 0.693). No significant differences were observed between MPV groups regarding age, menopausal status, tumor biomarkers, metastatic characteristics, or recurrence timing. In multivariable analysis, central nervous system metastasis was independently associated with increased mortality (HR 2.22, 95% CI: 1.224–4.027; p = 0.009), whereas MPV status was not independently associated with overall survival (HR 0.81, 95% CI: 0.379–1.750; p = 0.601).

Conclusion: Pretreatment MPV was not identified as an independent prognostic factor for overall survival in patients with recurrent or de novo metastatic breast cancer. Although MPV is an easily accessible hematological parameter, these findings indicate that MPV alone is unlikely to serve as a reliable prognostic biomarker in this clinical context. Further studies with larger cohorts, standardized MPV measurement methods, and adjustment for potential confounding factors are warranted.

Keywords: mean platelet volume, metastatic breast cancer, prognosis, overall survival

Introduction

Breast cancer is the most common cancer among women worldwide. The World Health Organization (WHO) reports that it is the leading cause of cancer deaths in women in less developed countries and the second leading cause in developed countries.[1,2] Treatments have moved beyond traditional options like surgery, radiotherapy, and chemotherapy to more personalized approaches, such as endocrine therapy, HER2-targeted therapy, CDK4/6 inhibitors, PARP inhibitors, antibody-drug conjugates,

https://doi.org/10.2147/BCTT.S629176
Received: 7 June 2026
Accepted: 7 July 2026
Published: 15 July 2026

© 2026 Gökdere et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v4.0) License (http://creativecommons.org/licenses/by-nc/4.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

immunotherapy, and other targeted treatments. Even with these advances, metastatic breast cancer is still mostly incurable. Survival rates depend on factors like tumor biology, the extent of metastasis, how the cancer responds to treatment, previous treatments, and patient-related inflammatory factors.[3] Because of this, there is ongoing interest in finding affordable and accessible biomarkers to help improve prognosis in recurrent or metastatic breast cancer.[4,5] The risk of recurrence is highest in the first two years after diagnosis, and most relapses happen within the first five years, though late recurrences can occur even after 20 years.[6] Prognosis can differ between de novo and recurrent metastatic breast cancer, but this often depends on the time without metastasis and tumor biology. Lobbezoo et al found that patients with de novo metastatic breast cancer had similar survival rates to those with recurrent metastatic breast cancer if the period without metastasis was longer than 24 months. However, patients with early recurrence had worse outcomes.[7] For all patients, clinical and survival data were collected from the time metastatic disease was diagnosed, and whether the disease was de novo or recurrent was included in the analysis.

Current clinical guidelines recommend several systemic treatment options for both recurrent and de novo metastatic breast cancer to prolong survival, control disease-related symptoms, and maintain quality of life. Prognosis in this context remains heterogeneous and is influenced by various clinical, pathological, and molecular factors, such as age, histological grade, hormone receptor status, HER2 expression, Ki-67 index, metastatic site and burden, vascular invasion, treatment sensitivity, and prior treatment exposure. Despite these complexities, there is ongoing clinical interest in inexpensive and easily accessible biomarkers that could refine prognostic assessment in recurrent or metastatic breast cancer.[5]

Platelet-related parameters, such as mean platelet volume (MPV), have garnered attention because platelet activation and systemic inflammation may contribute to tumor progression, metastatic dissemination, and interactions within the tumor microenvironment.[4–6] This study therefore evaluates MPV in patients with recurrent or de novo metastatic breast cancer to determine whether this routinely available hematological marker possesses clinically meaningful prognostic value in this specific setting.

Platelet function is closely related to platelet size, and mean platelet volume (MPV) is widely used as a simple indicator of average platelet size and platelet activation. MPV is routinely measured as part of complete blood count analysis using automated hematologic analyzers. However, its reference ranges may vary across laboratories because of differences in analytical equipment, sample handling, and measurement methods. Previous studies have suggested that MPV may be associated with angiogenesis, tumor progression, and prognosis in several malignancies.[8,9] In breast cancer, pretreatment MPV has also been linked to more aggressive clinicopathological features in some studies. Nevertheless, data regarding the prognostic significance of MPV in patients with recurrent or metastatic breast cancer remain limited and inconsistent. Therefore, evaluating the clinical and prognostic relevance of pretreatment MPV in this specific patient population may provide additional insight into its potential utility as an accessible and inexpensive biomarker.[10,11]

Platelet-related indices have recently attracted increasing attention in breast cancer research. Beyond conventional observational studies, genetic epidemiology approaches have been used to explore the potential causal relevance of platelet parameters. A recent Mendelian randomization and colocalization study reported suggestive evidence for associations between platelet indices, including plateletcrit, mean platelet volume, and platelet distribution width, and breast cancer risk. These findings support the biological relevance of platelet-related parameters in breast cancer, although their prognostic significance in patients with recurrent or de novo metastatic disease remains uncertain.[12]

Meta-analyses suggest pretreatment MPV may relate to cancer prognosis, but study heterogeneity limits firm conclusions.[13] For example, a retrospective study in China with 94 patients having locally advanced or metastatic breast cancer found no link between MPV and prognosis.[14] Conversely, another study reported that patients with liver metastasis had lower MPV values, suggesting a possible connection.[15] The prognostic significance of MPV in metastatic breast cancer remains unclear due to limited and inconsistent evidence, partly caused by variations in patient populations, disease stages, cutoff values, timing of MPV measurement, and outcome definitions.[14–16] This study aims to address this gap by examining the association between MPV levels and survival in patients with recurrent or metastatic breast cancer. If validated as a prognostic marker, this widely available and cost-effective test could guide treatment decisions.[13–16] Pretreatment MPV values were compared with patient survival and analyzed alongside established prognostic factors, including tumor characteristics (ER, PR, HER2 status), age, menopausal status, metastatic sites, and timing of recurrence.

Materials and Methods

Study Design and Patient Selection

This retrospective cohort study included 200 female patients with histologically confirmed recurrent or de novo metastatic breast cancer who were followed and treated at the Department of Medical Oncology, Ankara University Faculty of Medicine, between 2010 and 2019. Eligible patients were women aged 27–88 years who had either de novo metastatic disease at initial diagnosis or recurrent disease after prior treatment for early-stage breast cancer. Patients were excluded if essential clinical, pathological, survival, or laboratory data, including pretreatment MPV values, were unavailable. Clinical, pathological, and laboratory data were retrospectively collected from the institutional electronic medical record system.

Data Collection and Variable Definition

Data were collected on patient age, menopausal status at diagnosis, tumor immunohistochemical profile (estrogen receptor [ER], progesterone receptor [PR], and human epidermal growth factor receptor 2 [HER2] status), site and number of metastatic lesions, timing of recurrence, comorbidities, smoking status, date of diagnosis or recurrence, follow-up duration, survival status, and date of death. For each patient, pretreatment mean platelet volume (MPV) was recorded from the complete blood count obtained within 30 days prior to the initiation of systemic treatment for recurrent or de novo metastatic breast cancer. The MPV cutoff value was established based on the upper reference limit of the institutional laboratory, which was 10.5 fL at Ankara University Faculty of Medicine during the study period. This value was used as the predefined cutoff for MPV categorization, in alignment with previous studies utilizing laboratory-specific reference limits. Survival analyses were initially conducted using this laboratory-based cutoff, and clinical and pathological characteristics were compared between patients with MPV values below 10.5 fL and those with MPV values of 10.5 fL or higher. Overall survival was defined as the interval from the date of recurrent or de novo metastatic breast cancer diagnosis to death from any cause or the last follow-up. Additionally, receiver operating characteristic (ROC) curve analysis was performed to identify an alternative MPV cutoff value for mortality prediction. The ROC-derived MPV cutoff was 9.55 fL, and sensitivity, specificity, positive likelihood ratio, and Youden index were calculated.

Clinicopathologic Variables

The following variables were analyzed as potential prognostic factors:

i. Pattern of disease presentation: recurrent vs de novo metastatic
ii. Menopausal status: premenopause vs postmenopausal
iii. Pretreatment mean platelet volume (MPV) level: MPV <10.5 fL vs MPV ≥10.5 fL
iv. Pretreatment mean platelet volume (MPV) level: MPV <9.55 fL vs MPV ≥ 9.55 fL
v. Tumor immunohistochemical profile: ER, PR, HER2 positive vs negative
vi. Timing of recurrence: ≤2 years classified as early recurrence vs >2 years as late recurrence
vii. Site of metastatic lesions: Bone, Liver, Lung, Lymph nodes (supraclavicular, hilar, mediastinal, intra-abdominal), Central nervous system (CNS), Pleura/peritoneum
viii. Comorbidities: hypertension, diabetes mellitus type 2, hyperlipidemia, chronic kidney disease, hypothyroidism, rheumatoid arthritis, heart failure, venous insufficiency, osteoporosis

Statistical Analysis

Statistical analyses were performed using SPSS software (version 25.0; IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using visual methods, including histograms and Q–Q plots, and analytical tests, including the Kolmogorov–Smirnov and Shapiro–Wilk tests. Non-normally distributed continuous variables were summarized as median and interquartile range (IQR), whereas categorical variables were presented as frequencies and percentages.

Groups were compared using the Mann–Whitney *U*-test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. The comparison of clinicopathological characteristics between the MPV <10.5 fL and MPV ≥10.5 fL groups is presented.

Overall survival (OS) was defined as the interval from the date of metastatic disease diagnosis in patients with de novo metastatic disease or from the date of recurrence/metastatic relapse in patients with recurrent disease to death from any cause or last follow-up. The Kaplan–Meier method was used to evaluate the association between MPV status and OS, and survival curves were compared using the Log rank test. Median follow-up time was estimated using the reverse Kaplan–Meier method.

Univariable and multivariable Cox proportional hazards regression analyses were performed to identify factors associated with OS. The variables evaluated included age group (<65 versus ≥65 years), menopausal status, disease presentation (de novo metastatic versus recurrent breast cancer), time to recurrence (<2 versus ≥2 years), estrogen receptor (ER) status, progesterone receptor (PR) status, human epidermal growth factor receptor 2 (HER2) status, MPV status (<10.5 versus ≥10.5 fL), comorbidity status, and metastatic sites, including bone, lung, central nervous system, soft tissue, and pleural or peritoneal involvement. Variables deemed clinically relevant or statistically significant in univariable analysis were incorporated into the multivariable Cox regression model.

The institutional laboratory upper reference limit was initially used as the MPV cutoff value. In addition, receiver operating characteristic (ROC) curve analysis was performed to determine an exploratory alternative MPV cutoff for OS. Sensitivity, specificity, positive likelihood ratio, and Youden index were calculated. ROC analysis was performed using overall mortality status as the binary outcome to explore the discriminatory ability of pretreatment MPV. Survival was not dichotomized at a fixed time point, such as 3- or 5-year OS; therefore, the ROC-derived MPV cutoff was considered exploratory.

Among patients with recurrent disease, the disease-free interval was defined as the time from initial breast cancer diagnosis or primary surgery to recurrence/metastatic relapse. Patients with de novo metastatic disease were excluded from this analysis because they had metastatic disease at initial diagnosis and therefore had no disease-free interval. Because MPV was evaluated only at the time of recurrent or de novo metastatic disease diagnosis, disease-free interval in recurrent patients was analyzed as a clinical prognostic factor rather than as an MPV-related outcome.

A two-sided p-value <0.05 was considered statistically significant.

Ethical Approval

The study protocol was approved by the Ethics Committee of Ankara University Faculty of Medicine (Approval No. İ11-707-20; Date: January 15, 2021). Written informed consent was obtained from all patients. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Study Population and Baseline Characteristics

A total of 200 female patients with de novo metastatic or recurrent breast cancer were included in the analysis. The median age at diagnosis was 53.5 years (range, 27–88), with 49% being premenopausal. Patient groups were defined by disease course: 68% experienced recurrence after prior early-stage disease, and 32% presented with metastatic disease at initial diagnosis. The median follow-up was 62 months (95% CI: 55.66–68.34), during which 53.5% of patients died. For metastatic sites, bone was most common (62.5%), followed by liver (47%), lung (29%), lymph nodes (23.3%), central nervous system (24%), and pleura/peritoneum (14.2%). For receptor status, 84% had estrogen receptor (ER) positivity, 67.5% had progesterone receptor (PR) positivity, and 35.5% had HER2 positivity. Pretreatment mean platelet volume (MPV) values were <10.5 fL in 85% of patients and ≥10.5 fL in 15%. Demographic and clinical characteristics are summarized in Table 1.

Table 1 Baseline Demographic, Clinical, and Tumor Characteristics of the Study Cohort

Variable	Category	n (%)
Age	Median	53.5
	Range	27–88
Menopausal Status	Premenopausal	98 (49%)
	Postmenopausal	102 (51%)
Recurrence or Metastasis Status	Recurrence	136 (68%)
	Metastasis	64 (32%)
Death	Yes	107 (53.5%)
	No	93 (46.5%)
Metastasis Site	Bone	137 (62.5%)
	Pleura/Peritoneum	31 (14.2%)
	Lymph Node	51 (23.3%)
Visceral Metastasis	Liver	71 (47%)
	Lung	44 (29%)
	CNS	36 (24%)
ER Status	Positive	168 (84%)
	Negative	32 (16%)
PR Status	Positive	135 (67.5%)
	Negative	65 (32.5%)
HER2 Status	Positive	71 (35.5%)
	Negative	129 (64.5%)
Pre-treatment MPV	<10.5	170 (85%)
	≥10.5	30 (15%)

Abbreviations: ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; CNS, Central Nervous System; MPV, mean platelet volume.

Survival Outcomes Stratified by Mean Platelet Volume (MPV) Values

Patients were divided into two groups based on MPV before treatment: MPV < 10.5 fL (n = 170, 85%) and MPV ≥ 10.5 fL (n = 30, 15%). Table 2 shows their main clinical and pathological features. There were no significant differences between the groups for age, menopausal status, type of disease (recurrence or new metastasis), locations of metastasis, tumor type (ER, PR, HER2 status), other illnesses, or smoking history ($p < 0.05$ was the cutoff for significance).

Table 2 Clinicopathological Characteristics of Patients According to Pretreatment MPV Levels

Variable	MPV <10.5 fL (n=170)	MPV ≥10.5 fL (n=30)	p-value
Age, years, median (IQR) (min–max)	53 (44–62) (29–84)	54 (43–66) (27–88)	0.541
Menopausal status			0.285
Premenopausal, n (%)	86 (50.6)	12 (40)	
Postmenopausal, n (%)	84 (49.4)	18 (60)	
Recurrence or metastasis status			0.49
Recurrence present, n (%)	115 (67.6)	21 (70)	
Metastatic at diagnosis, n (%)	55 (85.9)	9 (14.1)	
Early recurrence, n (%)	32 (27.8)	5 (23.8)	0.704
Late recurrence, n (%)	83 (72.2)	16 (76.2)	0.704
Time to recurrence, years, median (IQR)	4 (2–8) (0.5–21)	4 (2.5–7) (0.3–11)	0.969
Number of metastatic sites, median (IQR) (min–max)	2 (1–2) (1–5)	1.5 (1–2) (1–5)	0.221

(*Continued*)

Table 2 (Continued).

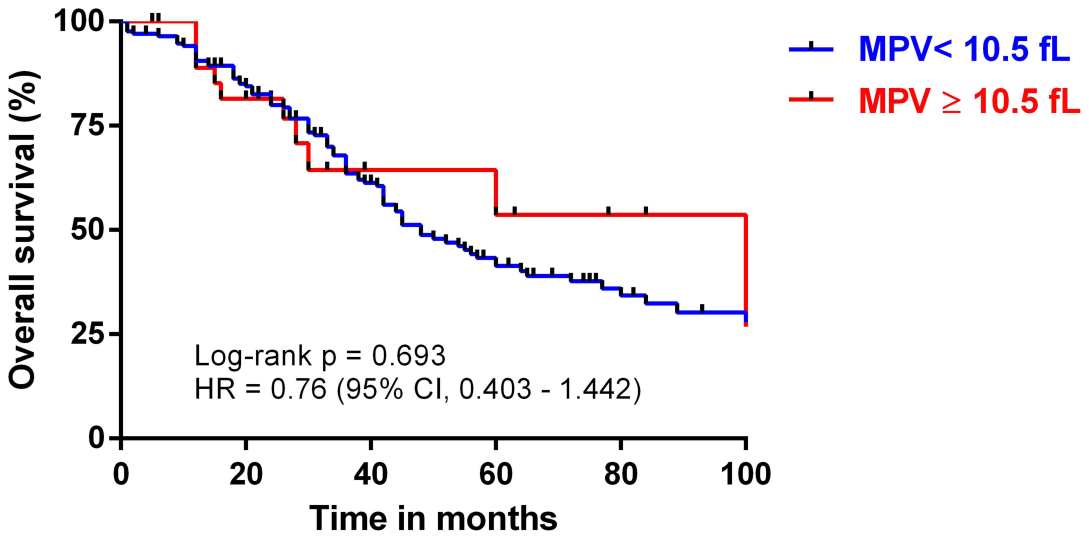
Variable	MPV <10.5 fL (n=170)	MPV ≥10.5 fL (n=30)	p-value
Metastatic site group			0.225
Single site, n (%)	65 (38.2)	15 (50)	
Multiple sites, n (%)	105 (61.8)	15 (50)	
Bone metastasis, n (%)	115 (67.6)	22 (73.3)	0.536
Pleura/Peritoneum metastasis, n (%)	28 (16.5)	3 (10)	0.583
Lung metastasis, n (%)	37 (21.8)	7 (23.3)	0.848
Lymph node metastasis, n (%)	44 (25.9)	8 (26.7)	0.768
Central nervous system (CNS) metastasis, n (%)	31 (18.2)	5 (16.7)	0.837
Liver metastasis, n (%)	63 (37.1)	8 (26.7)	0.273
ER positive, n (%)	140 (82.4)	28 (93.3)	0.178
PR positive, n (%)	114 (67.1)	21 (70)	0.751

Abbreviations: ER, estrogen receptor; PR, progesterone receptor; CNS, Central Nervous System; MPV, mean platelet volume; IQR, interquartile range.

The median overall survival was 54 months (95% CI: 28.9–79.1) for patients with recurrent disease and 44 months (95% CI: 32.7–55.3) for those with newly diagnosed metastatic disease. This difference did not reach statistical significance (p = 0.079).

Using an MPV cutoff of 10.5 fL, the median overall survival was 48 months (95% CI: 38.2–57.8) for patients with MPV less than 10.5 fL and 108 months (95% CI: 26.2–189.8) for those with MPV greater than or equal to 10.5 fL. This difference was not statistically significant (log-rank p = 0.693) (Figure 1).

A receiver operating characteristic (ROC) analysis was conducted to identify the optimal MPV threshold for predicting overall survival. The analysis indicated that an MPV cutoff of 9.55 fL provided the best predictive value,



Time (months)	0	20	40	60	80	100
MPV < 10.5 fL	170	138	82	44	21	14
MPV ≥ 10.5 fL	30	22	7	6	4	3

Figure 1 Overall survival by pretreatment MPV level Kaplan–Meier overall survival curve according to the predefined institutional MPV cutoff value of 10.5 fL. Overall survival was compared between patients with MPV <10.5 fL and those with MPV ≥10.5 fL.

https://doi.org/10.2147/BCTT.S629176

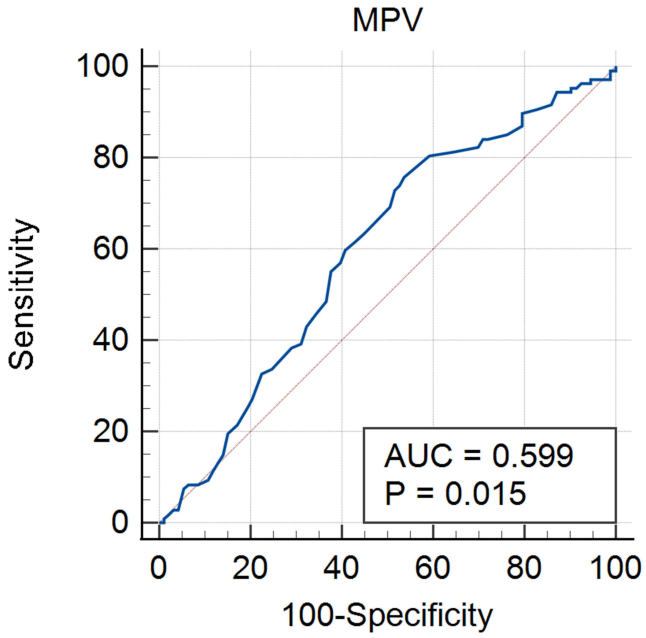


Figure 2 ROC curve analysis for calculating the optimal MPV cutoff value. ROC curve analysis for determining the optimal MPV cutoff value for mortality prediction. The ROC-derived optimal cutoff value was 9.55 fL, with an area under the curve of 0.599. Kaplan–Meier survival curve according to the ROC-derived MPV cutoff value. Kaplan–Meier curve showing overall survival according to the ROC-derived MPV cutoff value of 9.55 fL. Patients were stratified into two groups as MPV <9.55 fL and MPV ≥9.55 fL. Overall survival was defined as the time from diagnosis of recurrent or de novo metastatic breast cancer to death from any cause or last follow-up.

with a sensitivity of 75.7% and a specificity of 46.2%. The positive likelihood ratio was 1.41, and the Youden index was 0.22. The area under the curve (AUC) was 0.599 (95% CI: 0.519–0.679, p = 0.016) (Figure 2).

Survival analysis using the ROC cutoff showed that patients with MPV below 9.55 fL had a median overall survival of 45 months (95% CI: 37.4–52.6). Those with MPV above 9.55 fL had a median overall survival of 84 months (95% CI: 40.4–127.6). However, this difference was not statistically significant (log-rank p = 0.628) (Supplementary Material 1).

Univariable Cox regression analysis found no significant association between MPV status and overall survival. Specifically, patients with MPV below 10.5 fL had a similar risk of death as those with MPV at or above 10.5 fL (HR 0.883, 95% CI 0.472–1.654; p=0.698). Consistent with this finding, MPV status was also not significant in the multivariable analysis (HR 0.81, 95% CI 0.379–1.75; p=0.601). In contrast, early recurrence in the univariable analysis was associated with a much higher risk of death (HR 2.98, 95% CI 1.782–5.014; p<0.001). Additionally, central nervous system (CNS) metastasis was associated with worse overall survival in both univariable (HR 1.94, 95% CI 1.090–3.471; p=0.024) and multivariable analyses (HR 2.22, 95% CI 1.224–4.027; p=0.009). Conversely, soft tissue metastasis was associated with better overall survival in both univariable (HR 0.52, 95% CI 0.292–0.939; p=0.030) and multivariable analyses (HR 0.46, 95% CI 0.258–0.844; p=0.012). Although ER positivity showed a trend toward better survival after adjustment, this did not reach statistical significance (HR 0.60, 95% CI 0.313–1.162; p=0.131) (Table 3).

Table 3 Univariable and Multivariable Cox Regression Analysis for Overall Survival

Variables	Univariable HR [95% CI]	p-value	Multivariable HR [95% CI]	p-value
Age group				
<65	Ref		–	–
≥65	1.05 [0.590 −1.897]	0.850		
Menopause				
Pre	Ref		–	–
Post	1.02 [0.701–1.505]	0.890		

(*Continued*)

https://doi.org/10.2147/BCTT.S629176

Table 3 (Continued).

Variables	Univariable HR [95% CI]	p-value	Multivariable HR [95% CI]	p-value
HER2 status				
Negative	Ref		–	–
Positive	0.73 [0.423–1.283]	0.280		
ER status				
Negative	Ref		Ref	0.131
Positive	0.64 [0.339 −1.243]	0.192	0.60 [0.313 −1.162]	
PR status				
Negative	Ref		–	–
Positive	0.78[0.461–1.350]	0.387		
MPV Status				
< 10.5 fL	Ref	0.698	Ref	0.601
≥ 10.5 fL	0.883 [0.472–1.654]		0.81 [0.379–1.75]	
Time to recurrence				
Late recurrence	Ref	**<0.001**	–	–
Early recurrence	2.98 [1.782–5014]			
Recurrence or metastasis				
Recurrence present	Ref			
Metastatic at diagnosis	0.70 [0.480–1.048]	0.085	–	–
Bone metastasis				
No	Ref		–	–
Yes	1.38 [0.905–2.120]	0.134		
Lung metastasis				
No	Ref			
Yes	0.83 [0.526 −1.330]	0.450	–	–
CNS metastasis				
No	Ref		Ref	**0.009**
Yes	1.94 [1.090 −3.471]	**0.024**	2.22 [1.224–4.027]	
Soft tissue metastasis				
No	Ref		Ref	**0.012**
Yes	0.52 [0.292–0.939]	**0.030**	0.46 [0.258–0.844]	
Pleural/Peritoneal metastasis				
No	Ref		–	–
Yes	0.71[0.408 −1.259]	0.246		
Comorbidity				
No	Ref	0.636		
Yes	0.91[0.623 −1.336]			

Notes:: Data are presented as hazard ratios (HR) and 95% confidence intervals (95% CI). Bold values indicate statistically significant differences at a statistical significance level of ≤0.05.

Abbreviations: ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; CNS, Central Nervous System; MPV, mean platelet volume; WHO, World Health Organization; AUC, area under the curve; CI, confidence interval; CNS, central nervous system; ER, estrogen receptor; PR, progesterone receptor; fL: femtoliter; HER2, human epidermal growth factor receptor 2; MPV, mean platelet volume; ROC, receiver operating characteristic.

Discussion

The precise impact of mean platelet volume (MPV) on prognosis in metastatic breast cancer remains unclear, as few studies have investigated its association with various metastatic patterns. Existing evidence is limited, derived from heterogeneous study designs, and frequently yields inconsistent findings. The present study differs from previous research by employing a larger sample size, using a single-center cohort to ensure consistent care, and extending the follow-up period.[17,18]

Research shows that both genetic and non-genetic factors can influence platelet measurements, such as MPV. Larger platelets are usually considered more active and more likely to form clots, while smaller platelets may indicate higher platelet turnover or use.[19] These differences might explain why studies on MPV in cancer have had mixed findings. In addition, systematic reviews have found that MPV is only moderately accurate for diagnosing or predicting thromboinflammatory conditions, suggesting that MPV alone may not be a strong biomarker.[20]

Many studies have examined whether mean platelet volume (MPV) and other platelet indices can predict outcomes in breast cancer. Mantas et al found links between higher platelet indices and the prognosis of invasive ductal carcinoma.[21] Tanriverdi et al suggested that MPV might help predict isolated bone metastasis.[22] Yao et al reported that MPV could have prognostic value in early-stage breast cancer.[23] However, our results show that MPV is no longer a useful predictor once the cancer has spread. Other studies have found links between MPV, inflammation, tumor biology, and patients' responses to treatment.[24–26] The differences in these findings are probably due to variations in patient groups, cancer stages, lab methods, and cutoff values. Without a standardized way to measure and interpret MPV, it remains difficult to use it regularly for prognostication.

A 2023 meta-analysis found that higher mean platelet volume (MPV) was associated with a greater risk of metastasis, while lower MPV was associated with a better chemotherapy response.[15] One major challenge in understanding these results is the lack of a standard cutoff value for MPV. The reported thresholds vary widely, from 7.4 to 12.2 fL, and are often set using receiver operating characteristic (ROC) curve analyses. MPV reference intervals can vary depending on the hematological analyzer, calibration method, and sample processing before analysis. These differences make it hard to compare studies and help explain why cutoff values vary so much.[8,16,27] In this study, MPV was measured using both the upper reference limit from the institutional lab and a ROC-derived cutoff value to facilitate comparison with earlier research.[15]

These findings are consistent with earlier studies. Li et al found that patients with breast cancer liver metastases, especially those who were postmenopausal, HER2-positive, or triple-negative, had lower MPV levels.[13] In our study, we also saw lower MPV values in patients with more aggressive tumor types, such as ER-negative and HER2-positive disease. However, we did not find a significant difference in MPV between patients with and without liver metastases, possibly because there were few cases of liver metastasis in our group.

A retrospective study conducted in China with 94 patients diagnosed with advanced or metastatic breast cancer reported no association between elevated mean platelet volume (MPV) and overall survival or prognosis.[28] These findings are consistent with the present study, which similarly observed no significant difference. Gu et al identified a mean platelet volume (MPV) cutoff of 8.45 fL that differentiated benign breast disease from invasive breast cancer and suggested a potential association between higher MPV and distant metastasis. However, the limited number of metastatic cases in their study restricts the ability to assess the prognostic value of MPV in metastatic disease. These findings highlight the variability in current evidence and the limited utility of MPV as a prognostic biomarker in metastatic breast cancer.

We studied 200 patients with either recurrent or newly diagnosed metastatic breast cancer. For overall survival, we used both the laboratory upper reference limit and an ROC-derived MPV cut-off. Standard ROC analysis is suitable for binary outcomes, but it does not fully account for censoring or the time-dependent nature of survival data. Heagerty et al recommended using time-dependent ROC curves to better assess the prognostic value of markers in censored survival data.[29] Therefore, the MPV cut-off from standard ROC analysis in our study should be interpreted with caution. Future research should use time-dependent ROC analysis to better assess the prognostic value of MPV in patients with recurrent or metastatic breast cancer.

Mean platelet volume (MPV) is a parameter reflecting platelet size in blood tests. MPV did not demonstrate an association with overall survival, regardless of whether laboratory-based or receiver operating characteristic (ROC)-derived cut-off values were applied. Additionally, MPV showed no association with age, menopausal status, disease presentation (recurrent or newly diagnosed metastatic), time to recurrence, comorbidity profile, or smoking status. Although mean MPV values were lower in subgroups characterized by more aggressive disease, such as estrogen receptor (ER) negativity, central nervous system metastasis, and multiple metastatic sites, these differences did not influence survival outcomes.

Several methodological factors may account for the negative findings observed in this study. First, unmeasured confounding variables, including systemic inflammation, comorbidities, prior treatments, disease burden, infection, or concomitant medications, could have influenced mean platelet volume (MPV) levels and survival outcomes. Although multivariable Cox regression was conducted to adjust for available prognostic variables, residual confounding remains due to the retrospective study design.

Second, pre-analytical variability in mean platelet volume (MPV) measurement may have influenced the results. Several pre-analytical factors, such as the type of anticoagulant, sample temperature, and the interval between venipuncture and analysis, can affect MPV values. MPV is known to increase over time in EDTA-anticoagulated blood due to platelet swelling. Consequently, differences in sample processing times may introduce measurement variability. This challenge complicates the standardization of MPV measurements in retrospective studies. Furthermore, the lack of standardized MPV cutoffs across studies limits comparability and may contribute to inconsistent findings in the literature. Therefore, pre-analytical variability may have also contributed to the negative findings of the present study.[30]

Previous studies show that composite platelet indices can provide more useful prognostic information than MPV alone. For example, Tera et al found that both the MPV-to-platelet count and PDW-to-platelet count ratios were higher in breast cancer patients with metastatic disease. These ratios may be simple and affordable ways to predict disease progression and poor outcomes.[31] Takeuchi et al also reported that a higher PDW-to-platelet count ratio, rather than MPV alone, was linked to shorter disease-free survival in breast cancer. This supports the idea that composite platelet indices may be more helpful than single measures.[16]

Research in other types of cancer supports this idea as well. For instance, in pancreatic cancer, MPV alone did not predict outcomes, but the MPV-to-platelet count ratio was an independent factor linked to worse overall survival.[32] These results suggest that composite platelet indices may better reflect the balance between platelet activation and platelet count than MPV alone. Future studies on biomarkers should include MPV as part of these composite indices, rather than treating it as a single measure.

Several studies have explored how MPV changes over time during systemic treatment. However, there is still not much evidence about its value in predicting outcomes for recurrent or metastatic breast cancer. Earlier research showed that MPV can change during endocrine treatment. For instance, Karagöz et al found that MPV increased after tamoxifen therapy but did not change after anastrozole. More recently, Yoon et al examined blood biomarkers at different times in a large group of breast cancer patients who received neoadjuvant chemotherapy. They collected samples at diagnosis, after chemotherapy, after surgery, and again 6 to 12 months later. Their analysis using linear mixed-effects models showed that higher MPV was linked to worse survival, which suggests that repeated blood biomarker tests could be useful in breast cancer.[33,34] Future research should examine whether changes in MPV during the disease or treatment provide more useful prognostic information than simply measuring MPV at the start.

In the present study, ROC analysis yielded an AUC of 0.599, indicating weak discriminatory ability of pretreatment MPV for mortality prediction. Therefore, the ROC-derived cutoff should be interpreted as exploratory rather than as a clinically validated threshold. In addition, when the institutional laboratory upper reference limit of 10.5 fL was used as the predefined cutoff, the distribution of patients between the MPV groups was markedly unbalanced, with most patients classified in the MPV <10.5 fL group. This imbalance may have reduced the statistical power of the comparisons and limited the ability to detect a potential prognostic effect of MPV.

The relationship between MPV level and prognosis in breast cancer appears to be complex and may depend on disease stage, timing of MPV measurement, treatment exposure, and the cutoff value used. In the present study, the ROC-derived cutoff of 9.55 fL was associated with numerically longer OS in patients with MPV values above this threshold.

However, because the AUC was low, this finding should be interpreted as exploratory and should not be considered evidence that higher MPV is a favorable prognostic marker. In contrast, when the predefined institutional laboratory cutoff of 10.5 fL was used, MPV was not significantly associated with OS. Although MPV may reflect platelet activation, systemic inflammation, and tumor–host interactions involved in metastatic progression, these potential biological associations did not translate into an independent prognostic effect on OS in our cohort. Therefore, pretreatment MPV should not be interpreted as either a clearly favorable or unfavorable standalone prognostic marker in patients with recurrent or de novo metastatic breast cancer.

Although mean platelet volume (MPV) has previously been investigated as an inflammatory and prognostic marker in breast cancer and other malignancies, data specifically evaluating pretreatment MPV in patients with recurrent or de novo metastatic breast cancer remain limited. This study contributes to the literature by assessing MPV in this clinically relevant metastatic context. Nevertheless, the novelty and clinical applicability of these findings should be interpreted with caution, given the retrospective, single-center design, limited sample size, lack of external validation, low discriminatory performance in the receiver operating characteristic (ROC) analysis, unbalanced distribution of MPV subgroups, and the absence of an independent association between MPV and overall survival.

Study Strengths and Limitations

This study has several limitations. First, its retrospective design may have introduced selection and information bias. MPV levels can be affected by several clinical and preanalytical factors, including smoking, hypertension, diabetes mellitus, hyperlipidemia, obesity, cardiovascular disease, anticoagulant or antiplatelet therapy, and differences in laboratory methods or equipment. Because complete and consistent data on all potential confounders were not available, these factors could not be fully adjusted for.

Second, the study was designed to focus on overall survival. Therefore, PFS, DFS, ORR, and DCR analyses could not be performed because complete treatment-related data, response assessments, and follow-up information required for these endpoints were not available. As a result, treatment variables such as CDK4/6 inhibitor use, HER2-targeted therapy, immunotherapy, chemotherapy lines, endocrine therapy, and subsequent treatment strategies could not be incorporated into the multivariable model.

Finally, the ROC-derived MPV cutoff should be considered exploratory. Conventional ROC analysis does not account for censoring or the time-to-event nature of overall survival, and the AUC value of 0.599 indicates limited discriminatory ability. Therefore, the 9.55 fL cutoff should not be interpreted as a clinically definitive threshold. Future studies using time-dependent ROC analysis, larger cohorts, and standardized MPV measurement methods are needed to validate clinically meaningful cutoff values.

Future Perspectives

Future biomarker research in recurrent and metastatic breast cancer should move beyond single baseline hematologic parameters and incorporate more comprehensive multimodal approaches. MPV and other platelet-related biomarkers may be more informative when evaluated together with dynamic inflammatory markers, liquid biopsy technologies, molecular tumor characteristics, and treatment-related variables. Emerging approaches such as circulating cell-free DNA methylation analysis may improve non-invasive cancer detection and molecular monitoring,[35] while biosensor-based biomarker platforms may enable rapid and sensitive assessment of tumor- or host-related biomarkers.[36] In addition, personalized cancer vaccines and other individualized therapeutic strategies highlight the growing importance of integrating prognostic biomarkers with molecularly guided treatment approaches.[37] Therefore, MPV alone is unlikely to be sufficient as a standalone prognostic marker, and future studies should focus on biomarker models that combine hematologic, inflammatory, molecular, immunologic, and technology-based variables.

Beyond platelet activation and systemic inflammation, extracellular vesicles have emerged as important mediators of breast cancer progression and metastasis by facilitating intercellular communication within the tumor microenvironment. Therefore, MPV alone may be insufficient to reflect the broader biological complexity of metastatic breast cancer.[38]

Conclusion

In conclusion, pretreatment MPV was not identified as an independent prognostic factor for overall survival in patients with recurrent or de novo metastatic breast cancer. Although an exploratory ROC-derived cutoff suggested a possible survival difference, its discriminatory ability was limited, and this finding should therefore be interpreted with caution. These results indicate that MPV alone is unlikely to serve as a reliable prognostic biomarker in this clinical setting. Future prospective studies with larger and more homogeneous cohorts, standardized MPV measurement methods, longitudinal assessment of platelet-related biomarkers, and careful adjustment for potential confounding factors are needed to better define the clinical role of MPV and other platelet-related indices in recurrent and metastatic breast cancer.

Acknowledgments

We want to express our sincere gratitude to our colleagues in the Department of Medical Oncology at Ege University Hospital for their invaluable support and collaboration. We also thank the hospital administration for their continued assistance in facilitating this research.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. *CA Cancer J Clin*. 2025;75(1):10–45. doi:10.3322/caac.21871
2. Tang DD, Ye ZJ, Liu WW, et al. Survival feature and trend of female breast cancer: a comprehensive review of survival analysis from cancer registration data. *Breast*. 2025;79:103862. doi:10.1016/j.breast.2024.103862
3. Sonkin D, Thomas A, Teicher BA. Cancer treatments: past, present, and future. *Cancer Genet*. 2024;286-287:18–24. doi:10.1016/j.cancergen.2024.06.002
4. Cardoso F, Spence D, Mertz S, et al. Global analysis of advanced/metastatic breast cancer: decade report (2005-2015). *Breast*. 2018;39:131–138. doi:10.1016/j.breast.2018.03.002
5. Trapani D, Martins-Branco D, Curigliano G, et al. Updated treatment recommendations for systemic treatment: from the ESMO Metastatic Breast Cancer Living Guideline. *Ann Oncol off J Eur Soc Med Oncol*. 2025;36(11):1414–1418. doi:10.1016/j.annonc.2025.07.017
6. Colleoni M, Sun Z, Price KN, et al. Annual hazard rates of recurrence for breast cancer during 24 years of follow-up: results from the international breast cancer study group trials I to V. *J Clin Oncol off J Am Soc Clin Oncol*. 2016;34(9):927–935. doi:10.1200/JCO.2015.62.3504
7. Lobbezoo DJA, van Kampen RJW, Voogd AC, et al. Prognosis of metastatic breast cancer: are there differences between patients with de novo and recurrent metastatic breast cancer? *Br J Cancer*. 2015;112(9):1445–1451. doi:10.1038/bjc.2015.127
8. Chen X, Li J, Zhang X, et al. Prognostic and clinicopathological significance of pretreatment mean platelet volume in cancer: a meta-analysis. *BMJ Open*. 2020;10(10):e037614. doi:10.1136/bmjopen-2020-037614
9. Pyo JS, Sohn JH, Kang G. Diagnostic and prognostic roles of the mean platelet volume in malignant tumors: a systematic review and meta-analysis. *Platelets*. 2016;27(8):722–728. doi:10.3109/09537104.2016.1169265
10. Zhou L, Zhang Z, Tian Y, Li Z, Liu Z, Zhu S. The critical role of platelet in cancer progression and metastasis. *Eur J Med Res*. 2023;28(1):385. doi:10.1186/s40001-023-01342-w
11. Wojtukiewicz MZ, Sierko E, Hempel D, Tucker SC, Honn KV. Platelets and cancer angiogenesis nexus. *Cancer Metastasis Rev*. 2017;36(2):249–262. doi:10.1007/s10555-017-9673-1
12. Zhu Y, Wu J. Causal analysis of platelet indices and breast cancer, including estrogen receptor-specific subtypes: a mendelian randomization study. *Int J Womens Health*. 2025;17:3455–3467. doi:10.2147/IJWH.S540325
13. Li MM, Yue CX, Fu S, Zhang X, Zhao CJ, Wang RT. Platelet Volume Is Reduced In Metastasing Breast Cancer: blood Profiles Reveal Significant Shifts. *Cancer Manag Res*. 2019;11:9067–9072. doi:10.2147/CMAR.S221976
14. Lu YJ, Cui MT, Liang ZW, et al. Prognostic values of platelet-associated indicators in advanced breast cancer. *Transl Cancer Res*. 2019;8(4):1326–1335. doi:10.21037/tcr.2019.07.28
15. Detopoulou P, Panoutsopoulos GI, Mantoglou M, et al. Relation of Mean Platelet Volume (MPV) with cancer: a systematic review with a focus on disease outcome on twelve types of cancer. *Curr Oncol*. 2023;30(3):3391–3420. doi:10.3390/curroncol30030258
16. Takeuchi H, Abe M, Takumi Y, et al. The prognostic impact of the platelet distribution width-to-platelet count ratio in patients with breast cancer. *PLoS One*. 2017;12(12):e0189166. doi:10.1371/journal.pone.0189166
17. Bozan MB, Yazar FM, Kale IT, Topuz S, Bozan AA, Boran OF. Immature granulocyte count and delta neutrophil index as new predictive factors for axillary metastasis of breast cancer. *J Coll Physicians Surg–Pak JCPSP*. 2022;32(2):220–225. doi:10.29271/jcpsp.2022.02.220
18. Panova-Noeva M, Schulz A, Hermanns MI, et al. Sex-specific differences in genetic and nongenetic determinants of mean platelet volume: results from the gutenberg health study. *Blood*. 2016;127(2):251–259. doi:10.1182/blood-2015-07-660308
19. Handtke S, Thiele T. Large and small platelets-(When) do they differ? *J Thromb Haemost JTH*. 2020;18(6):1256–1267. doi:10.1111/jth.14788
20. Kovács S, Csiki Z, Zsóri KS, Bereczky Z, Shemirani AH. Characteristics of platelet count and size and diagnostic accuracy of mean platelet volume in patients with venous thromboembolism. A systematic review and meta-analysis. *Platelets*. 2019;30(2):139–147. doi:10.1080/09537104.2017.1414175

21. Mantas D, Kostakis ID, Machairas N, Markopoulos C. White blood cell and platelet indices as prognostic markers in patients with invasive ductal breast carcinoma. *Oncol Lett*. 2016;12(2):1610–1614. doi:10.3892/ol.2016.4760
22. Tanriverdi O, Menekse S, Teker F, et al. The mean platelet volume may predict the development of isolated bone metastases in patients with breast cancer: a retrospective study of the Young Researchers Committee of the Turkish Oncology Group (TOG). *J BUON off J Balk Union Oncol*. 2016;21(4):840–850.
23. Yao M, Liu Y, Jin H, et al. Prognostic value of preoperative inflammatory markers in Chinese patients with breast cancer. *Oncol Targets Ther*. 2014;7:1743–1752. doi:10.2147/OTT.S69657
24. Mutlu H, Eryılmaz MK, Musri FY, Gunduz S, Salim DK, Coskun HS. Mean platelet volume as an independent predictive marker for pathologic complete response after neoadjuvant chemotherapy in patients with locally advanced breast cancer. *Asian Pac J Cancer Prev APJCP*. 2016;17 (4):2089–2092. doi:10.7314/apjcp.2016.17.4.2089
25. Sun H, Yin CQ, Liu Q, Wang F, Yuan CH. Clinical significance of routine blood test-associated inflammatory index in breast cancer patients. *Med Sci Monit Int Med J Exp Clin Res*. 2017;23:5090–5095. doi:10.12659/msm.906709
26. Divsalar B, Heydari P, Habibollah G, Tamaddon G. Hematological parameters changes in patients with breast cancer. *Clin Lab*. 2021;67(8). doi:10.7754/Clin.Lab.2020.201103
27. Noris P, Melazzini F, Balduini CL. New roles for mean platelet volume measurement in the clinical practice? *Platelets*. 2016;27(7):607–612. doi:10.1080/09537104.2016.1224828
28. Gu M, Zhai Z, Huang L, et al. Pre-treatment mean platelet volume associates with worse clinicopathologic features and prognosis of patients with invasive breast cancer. *Breast Cancer*. 2016;23(5):752–760. doi:10.1007/s12282-015-0635-6
29. Heagerty PJ, Lumley T, Pepe MS. Time-dependent ROC curves for censored survival data and a diagnostic marker. *Biometrics*. 2000;56 (2):337–344. doi:10.1111/j.0006-341x.2000.00337.x
30. Lancé MD, van Oerle R, Henskens YMC, Marcus MAE. Do we need time adjusted mean platelet volume measurements? *Lab Hematol off Publ Int Soc Lab Hematol*. 2010;16(3):28–31.
31. Tera Y, Azzam H, Abousamra N, et al. Platelet activation and platelet indices as markers for disease progression in women with breast cancer: platelets and prognosis of breast cancer. *Arch Breast Cancer*. 2022. 346–353.
32. Gong X, Zhang L, Yang D, et al. Mean platelet volume/platelet count ratio is associated with prognosis in patients with pancreatic cancer. *Int J Clin Exp Med*. 2016;9(8):16379–16386.
33. Yoon TI, Baek S, Lee JH, et al. Clinical significance of peripheral blood parameters as a prognostic biomarker in patients receiving neoadjuvant chemotherapy for breast cancer. *BMC Cancer*. 2026;26(1):170. doi:10.1186/s12885-025-15510-0
34. Karagöz B, Bilgi O, Alacacioğlu A, et al. Mean platelet volume increase after tamoxifen, but not after anastrazole in adjuvant therapy of breast cancer. *Med Oncol*. 2010;27(2):199–202. doi:10.1007/s12032-009-9191-2
35. Dong W, Lau CH, Li J, et al. Pan-cancer methylation analysis of circulating cell-free DNA. *Cancer Genet*. 2025;296-297:182–195. doi:10.1016/j.cancergen.2025.07.014
36. Nimhan G, Narwade M, Gajbhiye K. Biosensor driven biomarker analysis: pioneering advancements in cancer diagnosis and therapeutic strategies. *Biomark Biochem Indic Expo Response Susceptibility Chem*. 2025;30(4):332–351. doi:10.1080/1354750X.2025.2515363
37. Iamukova L, Alferova E. Personalized Cancer Vaccines in the Clinical Trial Pipeline. *Asia Pac J Clin Oncol*. 2026;22(3):362–368. doi:10.1111/ajco.70006
38. Jahangiri L. The impact of extracellular vesicles on breast cancer metastasis and therapeutics: genetic considerations. *Cancer Genet*. 2025;298-299:1–9. doi:10.1016/j.cancergen.2025.08.003

Breast Cancer: Targets and Therapy

Dovepress
Taylor & Francis Group

Publish your work in this journal

Breast Cancer - Targets and Therapy is an international, peer-reviewed open access journal focusing on breast cancer research, identification of therapeutic targets and the optimal use of preventative and integrated treatment interventions to achieve improved outcomes, enhanced survival and quality of life for the cancer patient. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/breast-cancer—targets-and-therapy-journal