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Outcomes and Tolerability of Sacituzumab Govitecan in Routine Clinical Practice for Metastatic Triple-Negative and Hormone Receptor-Positive/HER2-Negative Breast Cancer

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ABSTRACT

Therapeutic options for patients with metastatic breast cancer become increasingly limited after multiple lines of systemic treatment. Sacituzumab govitecan (SG), a Trop-2–targeting antibody–drug conjugate, has been incorporated into treatment algorithms for metastatic triple-negative breast cancer and more recently for hormone receptor-positive/HER2-negative disease. However, evidence describing its performance in routine oncology practice remains sparse. This retrospective multicenter study examined real-world treatment outcomes, toxicity, and clinical factors associated with survival in patients receiving SG. Clinical records of 68 patients treated with SG between 2022 and 2025 at participating oncology centers in Turkey were analyzed. Patients with triple-negative disease had previously received at least one chemotherapy regimen, whereas those with hormone receptor-positive/HER2-negative disease had undergone endocrine therapy combined with CDK4/6 inhibition and a minimum of two prior chemotherapy lines. Treatment effectiveness was assessed using progression-free survival, overall survival, and radiologic response. Multivariable regression analyses were conducted to explore predictors of outcome. Safety data were collected and graded using CTCAE version 5.0 criteria. The study population consisted of 35 patients with triple-negative disease and 33 with hormone receptor-positive/HER2-negative disease. Survival outcomes were comparable between subgroups, with median progression-free and overall survival durations of 6.1 months and 12.5 months, respectively. Tumor response was observed in more than half of the cohort, including complete responses in a subset of patients. Poor functional status and the presence of hepatic metastases were independently associated with inferior survival outcomes. Previous exposure to immune checkpoint inhibitors did not compromise treatment benefit. Adverse events were generally manageable, with hematologic toxicity, gastrointestinal symptoms, and alopecia occurring most frequently. Permanent treatment cessation due to toxicity was uncommon. In a real-life clinical setting, SG demonstrated consistent activity and an acceptable safety profile across two major metastatic breast cancer subtypes. Although the observed outcomes align with those reported in prospective trials, the absence of a control group limits causal interpretation. Importantly, this analysis contributes early real-world evidence supporting the use of SG in hormone receptor-positive/HER2-negative metastatic breast cancer and highlights the need for further prospective and biomarker-driven research.

Keywords: Trop-2, Metastatic breast cancer, Antibody–drug conjugates, Sacituzumab govitecan, Hormone receptor-positive breast cancer, Real-world evidence

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Introduction

Breast cancer is the most commonly diagnosed cancer among women globally and continues to pose a major public health burden. Although advances in early detection and systemic therapies have improved outcomes, advanced-stage disease remains associated with significant morbidity and mortality [1, 2].

Hormone receptor-positive, HER2-negative metastatic breast cancer (mHRPBC) represents the largest molecular subtype, accounting for roughly 70% of cases. First-line management typically involves endocrine-based

strategies combined with targeted agents such as cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors. Despite initial responsiveness, many patients ultimately develop resistance to hormonal therapies, necessitating a transition to cytotoxic chemotherapy. In the metastatic setting, chemotherapy is frequently associated with modest survival gains, substantial toxicity, and deterioration in quality of life, with median overall survival rarely exceeding three years once endocrine resistance develops [3-5].

Triple-negative metastatic breast cancer (mTNBC), comprising approximately 10–15% of breast cancer diagnoses, is characterized by an aggressive biological behavior and a propensity for early disease progression and visceral dissemination, including involvement of the central nervous system. Owing to the absence of established molecular targets, systemic chemotherapy has historically remained the primary treatment option. However, therapeutic outcomes in this population remain poor, with limited progression-free survival (PFS) and overall survival (OS) following conventional regimens [6, 7].

Sacituzumab govitecan (SG) is a recently developed antibody–drug conjugate designed to target Trop-2, a transmembrane glycoprotein highly expressed across various epithelial malignancies, including both mTNBC and mHRPBC. The agent consists of a humanized monoclonal antibody directed against Trop-2, linked via a hydrolysable connector to SN-38, the active metabolite of irinotecan. This molecular design enables selective delivery of cytotoxic payloads to tumor cells while also exerting a bystander effect on adjacent malignant cells within the tumor microenvironment [8-12].

Following encouraging results from early clinical investigations, SG received accelerated approval from the United States Food and Drug Administration (FDA) in 2020 for patients with mTNBC who had previously undergone at least two lines of systemic therapy. Its clinical benefit was subsequently confirmed in the phase III ASCENT trial, which demonstrated superior survival and response outcomes compared with standard chemotherapy [13]. The therapeutic indication of SG was later expanded to include mHRPBC after the TROPiCS-02 trial showed improved outcomes versus physician-selected chemotherapy in heavily pretreated, endocrine-refractory patients [14].

Despite strong evidence from randomized controlled trials supporting the efficacy and safety of SG, data derived from routine clinical practice remain limited, particularly across heterogeneous patient populations and when evaluating both major Trop-2–expressing breast cancer subtypes. Real-world observational studies are therefore critical to better characterize treatment tolerability, utilization patterns, and prognostic variables outside the constraints of controlled trial environments [15-19].

Accordingly, this multicenter retrospective study was designed to evaluate and compare real-world clinical outcomes, safety, and prognostic factors associated with SG treatment in patients with mTNBC and mHRPBC. By incorporating both molecular subtypes, this analysis aims to provide a broader perspective on treatment performance and identify variables influencing response and survival in everyday clinical practice.

Materials and Methods

Patient selection and study design

This multicenter, retrospective observational study included 68 adult female patients diagnosed with either mTNBC or mHRPBC who were treated with sacituzumab govitecan between 2022 and 2025. Data were collected from multiple oncology centers. Eligible participants were required to be at least 18 years of age at the time of treatment initiation. Patients were assigned to the mTNBC cohort if disease progression had occurred following a minimum of one prior chemotherapy or chemoimmunotherapy regimen. Inclusion in the mHRPBC cohort required documented progression after at least two chemotherapy lines administered subsequent to treatment with CDK4/6 inhibitors and endocrine therapy. Exclusion criteria included prior treatment with SG within a clinical trial, a history of another primary malignancy within the preceding five years (with the exception of non-metastatic skin cancers), lack of informed consent, or male sex. Given its retrospective nature and the absence of a comparator arm, this study was not designed to assess the comparative efficacy of SG. Instead, its primary objective was to descriptively evaluate treatment outcomes and tolerability in a real-world clinical setting.

Therapeutic management

Sacituzumab govitecan therapy was delivered intravenously following standard dosing principles, with administrations on two separate days within each 21-day treatment cycle. The initial prescribed dose was 10 mg/kg. In patients who developed treatment-related toxicities, dose attenuation was implemented in a stepwise

manner, first reducing the dose to 7.5 mg/kg and subsequently to 5 mg/kg if required. To proactively reduce the risk of chemotherapy-induced neutropenia, granulocyte colony-stimulating factor (G-CSF) was frequently employed as a preventive measure. Treatment was continued as long as clinical benefit was observed and was discontinued upon radiographic or clinical disease progression, development of intolerable adverse effects, or patient preference.

Definition of endpoints

The main clinical endpoints evaluated in this study were progression-free survival (PFS) and overall survival (OS). PFS was defined as the duration between the initiation of sacituzumab govitecan and the first occurrence of documented disease progression or death, regardless of cause. OS was calculated from the start of SG therapy until death from any cause. Safety evaluation focused on identifying and grading treatment-related adverse events (AEs), which were classified according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0. Information regarding dose modifications and treatment discontinuation attributable to toxicity was systematically collected.

Analytical approach

All statistical procedures were conducted using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Baseline demographic and clinical variables were summarized descriptively. Categorical variables were presented as absolute numbers and proportions, while continuous variables were reported using either medians with ranges or means with standard deviations, depending on data distribution.

Time-to-event outcomes were analyzed using Kaplan–Meier survival estimates. Overall survival was measured from the date of first sacituzumab govitecan administration to the date of death. Survival curves were compared between predefined clinical categories using the log-rank (Mantel–Cox) test. These comparisons included molecular subtype classification (mTNBC versus mHRPBC), performance status as assessed by the Eastern Cooperative Oncology Group (ECOG PS 0 versus 1), and the presence of specific metastatic sites such as liver, bone, or central nervous system involvement.

To investigate potential prognostic variables, univariate analyses were performed for both PFS and OS, assessing the influence of baseline factors including tumor subtype, ECOG performance status, metastatic burden and distribution, prior systemic therapies, and Ki-67 proliferation index. Variables demonstrating statistical relevance in univariate testing were subsequently incorporated into multivariable Cox proportional hazards models to identify independent determinants of survival outcomes. Results were expressed as hazard ratios (HRs) with corresponding 95% confidence intervals (CIs). In addition, logistic regression analyses were applied to explore associations between clinical variables and objective treatment response. All statistical evaluations were two-sided, and statistical significance was defined by a p-value < 0.05.

Ethical compliance

The study was conducted in accordance with ethical principles governing human research and was approved by the institutional ethics committees of all participating centers. Specific approval was obtained from the Istanbul Medipol University Ethics Committee (Decision No. 1209, dated 28 November 2024). Prior to treatment initiation, written informed consent was obtained from all enrolled patients.

Results and Discussion

Patient characteristics at baseline

Baseline demographic and clinical features of the 68 patients analyzed are detailed in **Table 1**. The study population had a median age of 48 years, with ages ranging from 29 to 78 years. Most patients were in good functional condition at the time of SG initiation, with 70.6% classified as Eastern Cooperative Oncology Group performance status (ECOG PS) 0.

With respect to prior systemic treatment exposure, nearly all patients had previously received taxane-based chemotherapy (94.1%), and a large proportion had been treated with anthracyclines (79.4%). De novo metastatic presentation was observed in approximately one-quarter of the cohort (26.5%). Based on tumor subtype, the population was almost evenly divided, with 35 patients (51.5%) diagnosed with metastatic triple-negative breast

cancer and 33 patients (48.5%) with hormone receptor-positive/HER2-negative metastatic disease. HER2 expression was most commonly absent, with immunohistochemistry scores of 0 reported in 70.4% of cases.
In the metastatic treatment setting, 42.6% of patients had received three or fewer prior lines of systemic therapy, whereas more than half (55.9%) had been treated with over three previous regimens. Metastatic involvement most frequently affected lymph nodes (85.3%), followed by bone and lung metastases (each 57.4%). Liver metastases were present in 51.5% of patients, and central nervous system involvement was documented in 42.6%.
Regarding exposure to sacituzumab govitecan, patients received a median of seven treatment cycles, with the number of cycles ranging from 3 to 37. Prophylactic administration of granulocyte colony-stimulating factor was employed in the majority of cases (88.2%) to support treatment tolerance.

Table 1. Baseline characteristics.

Characteristic	Value
Median Age (Range)	48 years (29–78)
De Novo Metastasis	18 patients (26.5%)
Molecular Subtype	
Metastatic Hormone Receptor-Positive/HER2-Negative (mHRPBC)	33 patients (48.5%)
Metastatic Triple-Negative Breast Cancer (mTNBC)	35 patients (51.5%)
ECOG Performance Status	
1	20 patients (29.4%)
0	48 patients (70.6%)
HER2 Status	
HER2 2+ (FISH Negative)	6 patients (8.8%)
HER2 1+	10 patients (14.7%)
HER2 0	52 patients (76.4%)
Sites of Metastasis	
Lung	39 patients (57.4%)
Liver	35 patients (51.5%)
Bone	39 patients (57.4%)
Brain	29 patients (42.6%)
Lymph Nodes	58 patients (85.3%)
Dose Reduction Due to Adverse Effects	20 patients (29.4%)
Previous Immunotherapy	22 patients (32.4%)
Treatment Discontinuation Due to Adverse Effects	2 patients (2.9%)
Number of Prior Therapy Lines in Metastatic Setting	
>3 Lines	38 patients (55.9%)
≤3 Lines	29 patients (42.6%)
Prior Exposure to Chemotherapy Agents	
Anthracycline	54 patients (79.4%)
Capecitabine	53 patients (77.9%)
Taxane	64 patients (94.1%)
Carboplatin	48 patients (70.6%)
Prior Local Therapy	60 patients (88.2%)
Granulocyte Colony-Stimulating Factor (G-CSF) Use with SG	60 patients (88.2%)
Median Number of Sacituzumab Govitecan Cycles (Range)	7 (3–37)

mHRPBC: metastatic hormone receptor-positive/human epidermal growth factor receptor 2-negative breast cancer, mTNBC: metastatic triple-negative breast cancer, FISH: fluorescence in situ hybridization, ECOG PS: Eastern Cooperative Oncology Group Performance Status, G-CSF: granulocyte colony-stimulating factor, SG: sacituzumab gavitecan.

Efficacy results

Following a median observation period of 6.8 months (95% CI: 5.4–10.0), the overall cohort achieved a median progression-free survival of 6.1 months (95% CI: 4.83–7.43) and a median overall survival of 12.5 months (95% CI: 9.92–15.07) (illustrated) **(Figures 1 and 2).**

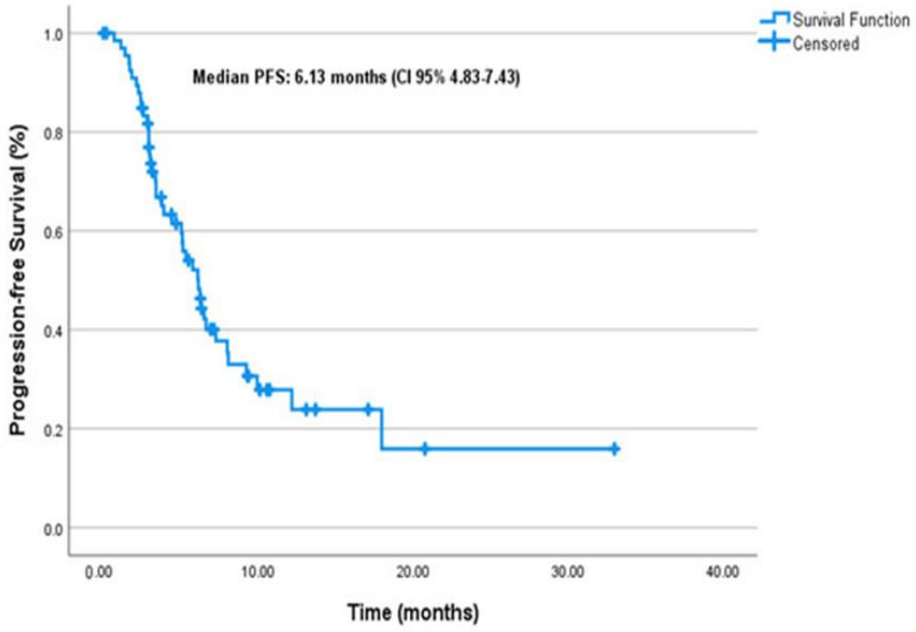

Figure 1. Progression-free survival

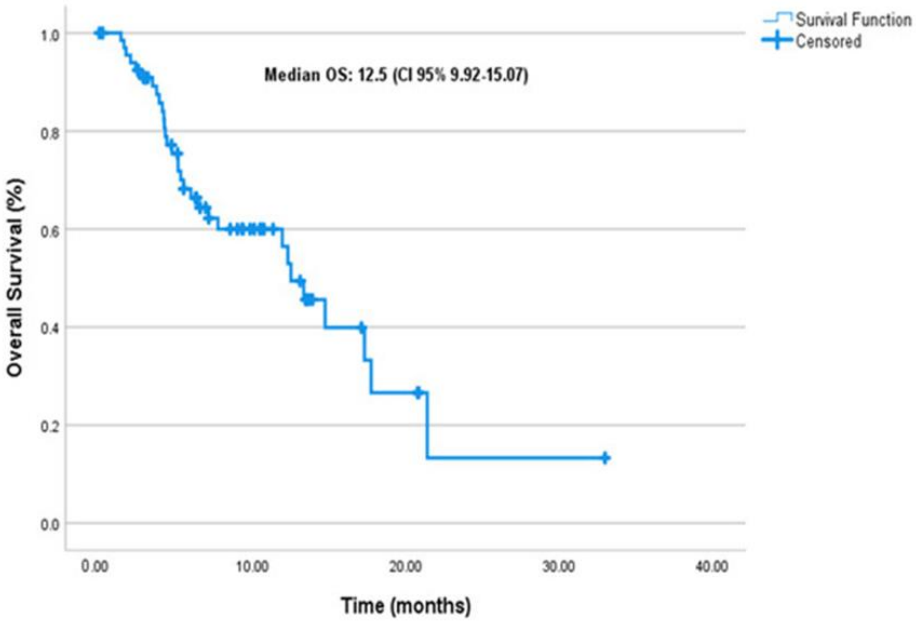

Figure 2. Overall survival.

No statistically significant differences in progression-free survival (PFS) were noted between the two molecular subtypes, with median PFS of 6.5 months in the mTNBC group and 5.76 months in the mHRPBC group (p = 0.78) **(Figure 3).**

Likewise, the presence of de novo metastatic disease did not significantly influence PFS (p = 0.63). In contrast, Eastern Cooperative Oncology Group Performance Status (ECOG PS) emerged as a significant prognostic factor, whereby patients with ECOG PS 0 experienced substantially longer PFS than those with ECOG PS 1 (p = 0.004).

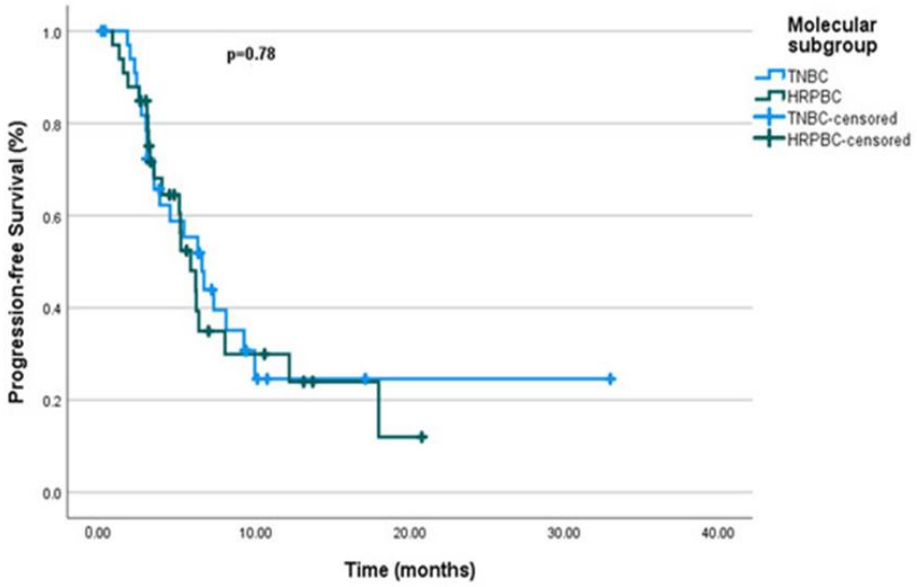

Figure 3. Progression-free survival stratified by molecular subtype.

The presence of liver metastases was associated with a significantly reduced PFS (p = 0.002). Similarly, bone metastases negatively influenced PFS (p = 0.004). In contrast, lung metastases (p = 0.088), brain metastases (p = 0.253), and lymph node metastases (p = 0.086) did not demonstrate statistically significant effects on PFS.

Prior exposure to immunotherapy showed no notable impact on PFS (p = 0.886). Previous treatment with specific chemotherapeutic agents—including taxanes, anthracyclines, carboplatin, and capecitabine—as well as prior local therapy or the number of metastatic therapy lines, also failed to reveal any significant associations with PFS.

Analysis of Ki-67 proliferation index revealed no significant difference in PFS between patients with Ki-67 ≤ 20% and those with Ki-67 > 20% (p = 0.897). Ki-67 levels assessed in metastatic biopsies likewise showed no correlation with PFS outcomes.

Furthermore, neither dose reductions necessitated by toxicity (p = 0.270) nor the prophylactic or therapeutic use of granulocyte colony-stimulating factor (G-CSF) (p = 0.097) significantly affected PFS.

Overall, these results identify Eastern Cooperative Oncology Group Performance Status (ECOG PS), liver metastases, and bone metastases as key factors adversely affecting progression-free survival, whereas prior treatment modalities, chemotherapy histories, and Ki-67 expression levels appear to have limited prognostic influence in this cohort **(Table 2).**

Table 2. Multivariate and univarate analyses of factors influencing progression-free survival.

Variable	Subgroup	mPFS (Months)	95% CI	p-Value	Multivariate p-Value	HR (95% CI)
Molecular subgroup				0.78	0.348	
	mTNBC	6.5	(4.45–8.54)			0.73 (0.384–1.401)
	mHRPBC	5.76	(4.28–7.24)			Ref.
ECOG PS				0.004	0.050	
	ECOG PS-1	3.76	(2.26–5.27)			1.96 (0.999–3.875)
	ECOG PS-0	7.26	(5.32–9.21)			Ref.
De novo metastases				0.63		
	Present	5.13	(1.97–8.28)			
	Absent	6.13	(4.71–7.88)			
Lung metastases				0.088		
	Present	3.9	(2.30–7.76)			
	Absent	8.0	(6.19–9.80)			
Liver metastases				0.002	0.047	

	Present	4.43	(2.74–6.12)			2.04 (1.008–4.151)
	Absent	NR	(4.83–7.43)			Ref.
Bone metastases				0.004	0.095	
	Present	5.03	(3.18–6.88)			1.87 (0.89–3.91)
	Absent	NR	NA			Ref.
Brain metastases				0.253		
	Present	5.03	(2.74–6.12)			
	Absent	6.50	(5.44–7.55)			
Lymph node metastases				0.086		
	Present	6.50	(4.07–8.92)			
	Absent	5.33	(4.31–6.35)			
Prior ICIs				0.886		
	Present	6.30	(2.31–10.28)			
	Absent	6.10	(4.89–7.30)			
No. of chemotherapy lines				0.796		
	>3 lines chemotherapy	6.23	(5.32–7.14)			
	≤3 lines chemotherapy	5.33	(2.89–7.76)			
Prior chemotherapy				0.352		
	Antracycline	6.13	(4.79–7.47)			
	Taxane	6.13	(4.86–7.40)			
	Capecitabine	6.13	(4.94–7.32)			
	Carboplatin	6.23	(4.62–7.84)			
Local treatment				0.929		
	Present	6.13	(4.90–7.36)			
	Absent	3.40	(0.10–11.71)			
G-CSF use with SG				0.097		
	Present	NR	NA			
	Absent	NR	NA			
Dose reduction due to toxicity				0.270		
	Absent	6.23	(5.33–7.13)			
	Present	3.13	(0.13–6.13)			
Metastatic setting Ki-67				1		
	>20	6.23	(4.67–7.79)			
	≤20	6.13	(3.46–8.80)			
At diagnosis Ki-67				0.897		
	>20	5.76	(4.27–7.25)			
	≤20	6.13	(4.55–7.71)			

MTNBC: metastatic breast cancer, triple-negative; mHRPBC: metastatic breast cancer, hormone receptor-positive/human epidermal growth factor receptor 2-negative; ECOG PS: performance status, Eastern Cooperative Oncology Group; G-CSF: colony-stimulating factor, granulocyte; ICIs: inhibitors, immune checkpoint; HR: ratio, hazard; CI: interval, confidence; NR: reached, not; NA: applicable, not; mPFS: progression-free survival, median; Ref: category, reference

Multivariate analysis assessed independent factors predicting progression-free survival (PFS). It revealed that the presence of liver metastasis markedly raised the risk of progression (HR = 2.046; p = 0.047), resulting in quicker disease advancement among affected patients. ECOG performance status similarly correlated with shortened PFS and more rapid progression (HR = 1.968; p = 0.050). By comparison, bone metastasis and molecular subtype failed to reach statistical significance in influencing PFS (p = 0.095 and p = 0.348, respectively) **(Table 2).**
Additionally, univariate analysis showed no notable difference in overall survival (OS) across molecular subgroups, specifically metastatic triple-negative breast cancer (mTNBC) and metastatic hormone receptor-

positive breast cancer (mHRPBC) (p = 0.38). Median OS stood at 11.93 months (95% CI: 5.22–18.64 months) in the mTNBC group and 11.3 months (95% CI: 9.16–25.4 months) in the mHRPBC group **(Figure 4).**

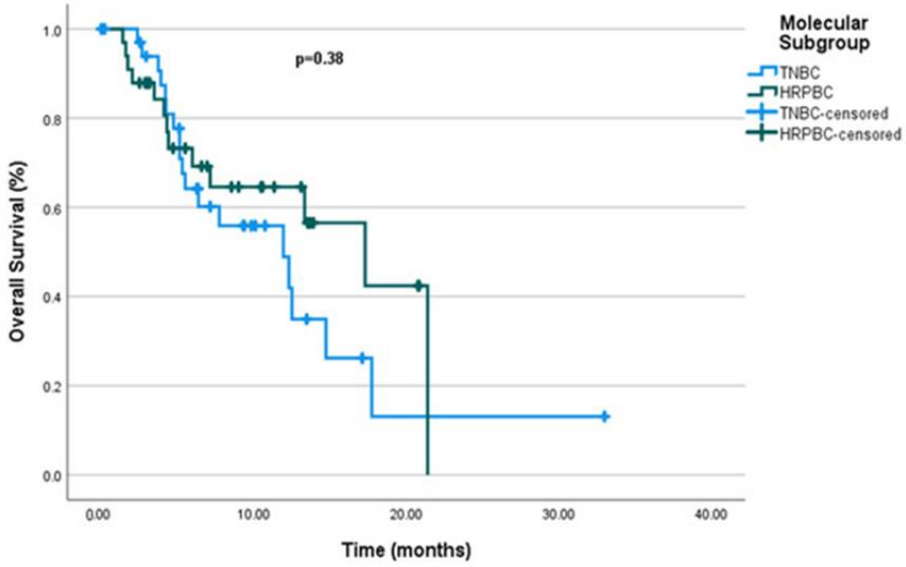

Figure 4. Overall survival stratified by molecular subtype.

Analysis of patients presenting with de novo metastatic disease revealed no evidence of survival heterogeneity, with a median overall survival (OS) of 14.73 months (95% CI: 4.23–25.23; p = 0.716). Functional status, as measured by ECOG performance score, was not a determinant of OS (p = 0.178).

Prognosis was strongly influenced by the pattern of metastatic spread. Hepatic involvement conferred the poorest outcome, reducing median OS to 5.96 months (p = 0.001). Survival was also significantly compromised in the presence of skeletal or intracranial metastases, with median OS of 11.93 months (p = 0.008) and 7.13 months (p = 0.02), respectively. Pulmonary metastases, however, were not associated with a statistically significant survival disadvantage (p = 0.076).

When treatment strategies were examined, only platinum-based therapy with carboplatin demonstrated a measurable survival advantage, extending median OS to 12.30 months (p = 0.04). No survival benefit was observed with other systemic therapies, including immune checkpoint inhibition or anthracycline-containing regimens (all p > 0.05).

Variables related to treatment exposure and tolerability—including the total number of chemotherapy lines, cessation of therapy due to adverse events, and prophylactic or therapeutic use of G-CSF—did not significantly alter OS outcomes. Likewise, tumor proliferative activity assessed by Ki-67 showed no association with survival, either at the time of initial diagnosis or following metastatic recurrence **(Table 3).**

Table 3. Multivariate and univariate predictors of overall survival.

Variable	Univariate p-Value	HR (95% CI)	Median OS (Months)	95% CI	Multivariate p-Value
Molecular subgroup	0.380				0.046
mTNBC		0.46 (0.22–0.98)	11.93	5.22–18.64	
mHRPBC		Ref.	11.30	9.16–25.4	
De novo metastases	0.716				
Present			14.73	4.23–25.23	
Absent			12.50	10.78–14.21	
Liver metastases	0.001				0.022
Present		3.15 (1.184–8.383)	5.96	2.79–9.14	
Absent		Ref.	17.73	Not available	Ref.

ECOG Performance Status	0.178				
ECOG 1			13.33	2.56–24.10	
ECOG 0			14.73	10.52–18.94	
Brain metastases	0.025				0.429
Present		1.39 (0.609–3.205)	7.13	1.07–13.18	
Absent		Ref.	17.30	11.12–23.47	
Lung metastases	0.076				
Present			7.13	3.65–14.78	
Absent			17.30	11.29–23.31	
Lymph node metastases	0.884				
Present			12.50	10.72–14.27	
Absent			21.40	Not available	
Bone metastases	0.008				0.073
Present		2.28 (0.927–5.624)	11.93	4.98–18.88	
Absent		Ref.	Not reached	Not available	Ref.
Prior chemotherapy	0.293				
Anthracycline			13.33	4.56–22.10	
Taxane			—	—	
Capecitabine			12.50	9.95–15.04	
Carboplatin			12.30	4.71–19.88	
Prior immune checkpoint inhibitors	0.963				
Present			12.50	10.31–14.68	
Absent			14.73	4.89–24.57	
Number of chemotherapy lines	0.745				
>3 lines			12.30	5.81–18.79	
≤3 lines			14.73	4.99–24.47	
Local treatment	0.673				
Present			12.50	10.75–14.24	
Absent			6.36	0.10–16.03	
G-CSF use with SG	0.724				
Present			13.33	6.96–19.69	
Absent			12.30	0.10–24.75	
Dose reduction due to toxicity	1.00				
Present			Not reached	Not available	
Absent			12.50	10.70–14.29	
Ki-67 in metastatic setting	0.184				
>20%			12.50	10.82–14.17	
≤20%			14.73	2.81–30.21	
Ki-67 at diagnosis	0.460				
>20%			12.30	6.02–18.57	
≤20%			14.73	4.85–22.63	

MTNBC: Metastatic triple-negative breast cancer; mHRPBC: Metastatic HER2-negative / hormone receptor-positive breast cancer; ECOG PS: Performance status according to Eastern Cooperative Oncology Group; G-CSF: Colony-stimulating factor for granulocytes; ICIs: Checkpoint inhibitors of the immune system; HR: Ratio of hazards; CI: Interval of confidence; NR: Not attained; NA: Not relevant; mOS: Median survival overall; Ref: Category used as reference

In the multivariate model evaluating overall survival (OS), metastatic involvement of the liver emerged as a key adverse prognostic factor, associated with a more than threefold increase in mortality risk (HR = 3.150; 95% CI: 1.184–8.383; p = 0.022) **(Table 3)**. Bone metastasis was linked to poorer survival outcomes but did not reach conventional statistical significance (HR = 2.283; 95% CI: 0.927–5.624; p = 0.073). Tumor molecular classification also independently influenced OS, with patients in the mTNBC subgroup demonstrating improved survival relative to those with mHRPBC (HR = 0.467; 95% CI: 0.221–0.987; p = 0.046). By contrast, the presence of brain metastases was not associated with OS after adjustment for other variables (HR = 1.398; 95% CI: 0.609–3.205; p = 0.429). Taken together, liver metastasis and molecular subtype remained independent determinants of OS in the final multivariate model **(Table 3).**

Tumor response was assessable in 68 patients. Objective responses were achieved in 52.9% of cases, including complete responses in 7 patients (10.3%) and partial responses in 29 patients (42.6%). Stable disease was documented in 14.7% of patients, resulting in an overall disease control rate of 67.6%.

To explore factors associated with treatment efficacy, a binary logistic regression analysis was performed **(Figure 5).** The likelihood of achieving an objective response was significantly higher in patients with liver metastases (OR = 6.49; p = 0.038) and lung metastases (OR = 7.59; p = 0.013). Bone metastases showed a borderline association with increased response probability (OR = 4.35; p = 0.050). In contrast, lymph node involvement was strongly associated with reduced treatment response (OR = 0.065; p = 0.017). No significant associations with response were observed for de novo metastatic presentation, molecular subtype, ECOG performance status, brain metastases, or Ki-67 expression (all p > 0.05) **(Figure 5).**

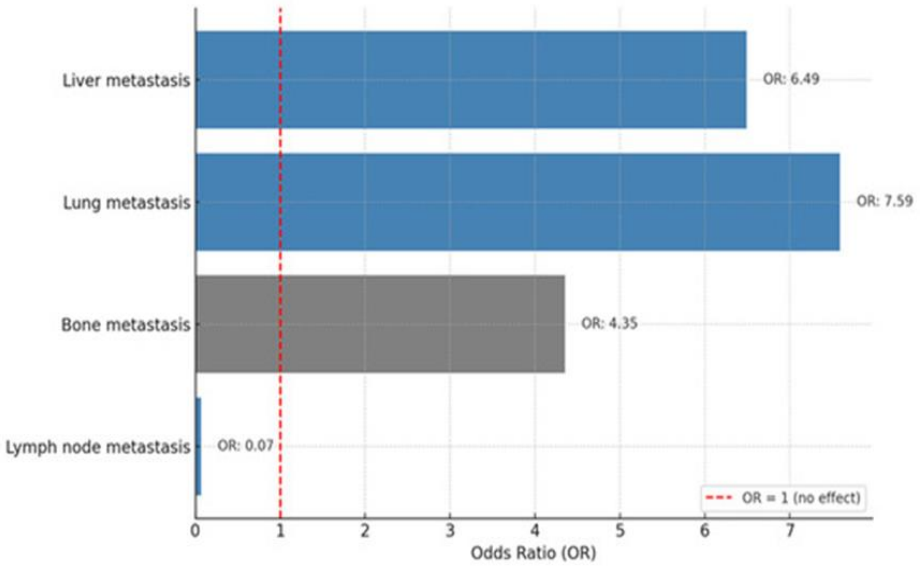

Figure 5. Factors associated with treatment response.

Adverse and safety events

The safety profile of treatment is summarized in **Figure 6**. Hair loss was the most frequently observed adverse event, affecting 90% of patients. Anemia was reported in 41.7% of the cohort, with severe cases (grade ≥3) occurring in 15%. Other hematologic toxicities, notably neutropenia and thrombocytopenia, were commonly encountered, and a considerable proportion reached grade ≥3 severity. These findings underscore the need for close laboratory surveillance and timely supportive interventions. In this context, primary prophylactic administration of granulocyte colony-stimulating factor (G-CSF) was implemented in 88.2% of patients to prevent or reduce neutropenia, highlighting its central role in managing SG-related hematologic toxicity.

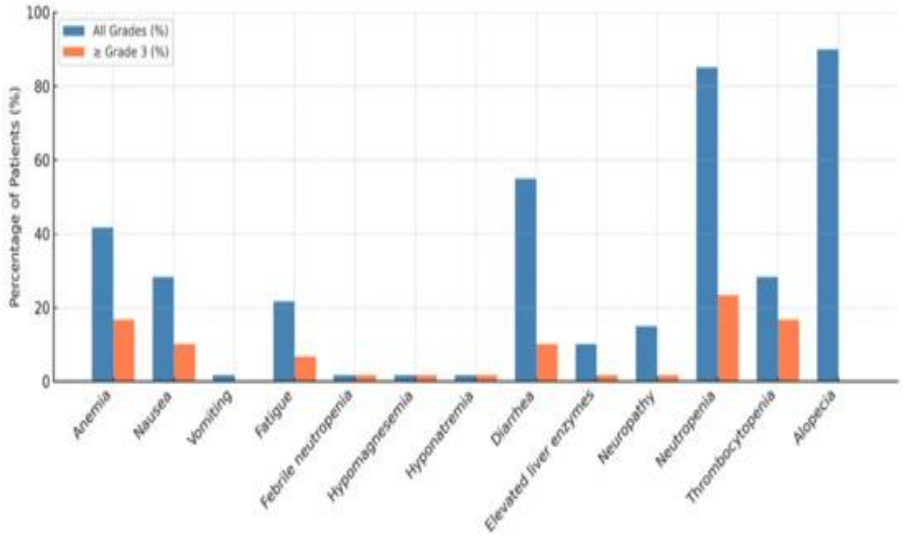

Figure 6. Adverse events.

Among non-hematologic adverse events, gastrointestinal symptoms were predominant. Nausea and diarrhea were the most frequently reported. Patients who developed nausea or vomiting of grade 2 or higher received standardized antiemetic prophylaxis, including dexamethasone, 5-hydroxytryptamine-3 (5-HT3) receptor antagonists, and neurokinin-1 (NK-1) receptor inhibitors. Diarrhea of grade ≥2 severity was treated promptly with antidiarrheal medications, reflecting an anticipatory strategy for gastrointestinal side-effect management. Fatigue was documented in 21.7% of patients, although high-grade fatigue was uncommon. Elevations in hepatic transaminases and episodes of febrile neutropenia were rare and did not necessitate interruption of therapy.

Treatment adjustments due to toxicity were required in a subset of patients. Dose reductions were implemented in 29.4% of cases, while permanent discontinuation of therapy occurred in 2.9% of patients, attributable to persistent grade 4 thrombocytopenia unresponsive to supportive measures. Collectively, these observations emphasize the importance of early detection and proactive management of adverse events to maintain treatment adherence and optimize therapeutic outcomes.

Real-world experience versus trial-based evidence

The present multicenter, retrospective analysis offers an observational snapshot of sacituzumab govitecan (SG) use in everyday oncology practice among patients with metastatic triple-negative breast cancer (mTNBC) and metastatic hormone receptor–positive/HER2-negative breast cancer (mHRPBC) treated in Turkey. Rather than serving as a measure of comparative efficacy, the findings aim to contextualize clinical outcomes and tolerability patterns observed outside the controlled environment of randomized trials. While median progression-free survival (PFS) and overall survival (OS) in this cohort fall within ranges reported in pivotal studies, these results should be viewed as descriptive reflections of real-world practice rather than confirmatory evidence of therapeutic effectiveness [20, 21].

In this population, median PFS reached 6.1 months and median OS was 12.5 months. These values align broadly with outcomes from landmark trials evaluating SG. In the ASCENT study, patients with heavily pretreated mTNBC achieved a median PFS of 5.6 months and an OS of 12.1 months [13]. Similarly, the TROPiCS-02 trial reported a median PFS of 5.5 months and OS of 14.4 months in mHRPBC patients [14]. Results from the EVER-132-002 trial, conducted in an Asian population, further corroborated SG activity, reporting a median OS of 21.0 months in the SG arm [22]. Despite these parallels, the absence of randomization and a control arm in the current study necessitates cautious interpretation.

A distinguishing feature of this analysis is the substantial representation of patients with mHRPBC, a group for which real-world outcome data remain notably scarce. To date, observational studies examining SG have largely concentrated on mTNBC, leaving hormone receptor–positive disease underrepresented despite emerging trial evidence supporting SG in this setting [16, 23]. To our knowledge, this study constitutes the first real-life cohort to concurrently and systematically examine SG outcomes in both mTNBC and mHRPBC populations.

Patients with mHRPBC accounted for nearly half of the cohort (48.5%, n = 33) and had uniformly received prior CDK4/6 inhibitor–based endocrine therapy as well as at least two lines of chemotherapy. In this subgroup, median PFS and OS were identical to those observed in the overall cohort (6.1 and 12.5 months, respectively), closely approximating the results of the TROPiCS-02 trial (median PFS 5.5 months; OS 14.4 months) [14]. These findings suggest that SG maintains clinically relevant activity in chemotherapy-pretreated mHRPBC patients beyond the confines of clinical trials.

The relevance of these observations is reinforced by data from EVER-132-002, which demonstrated favorable efficacy and safety of SG in Asian patients with mHRPBC [22]. However, outside of trial settings, published real-world evidence focusing specifically on this subgroup remains extremely limited. As such, the current study adds incremental observational data that may help guide treatment decisions in endocrine-resistant, heavily pretreated mHRPBC patients.

From a prognostic perspective, functional status and disease distribution emerged as critical determinants of outcome. In multivariate analyses, an ECOG performance status ≥1 and the presence of liver metastases were independently associated with inferior PFS and OS. These findings mirror prior real-world analyses and clinical trial substudies identifying compromised performance status and visceral disease as markers of poor prognosis [24-26]. Notably, ECOG performance status retained independent significance for OS, underscoring the central role of baseline patient condition in shaping treatment outcomes.

Among metastatic sites, hepatic involvement consistently signaled an unfavorable prognosis. This observation aligns with evidence from the ASCENT trial and a meta-analysis demonstrating attenuated benefit from SG in patients with liver metastases [25]. Comparable trends have also been documented in Italian and Polish real-world cohorts, further substantiating the adverse prognostic impact of liver metastasis across diverse populations [16, 23].

Paradoxically, despite their association with shortened survival, both liver and lung metastases were independently linked to higher objective response rates in this cohort. One potential explanation is that SG induces rapid tumor regression in highly vascularized organs, resulting in early radiographic responses that are not sustained over time. Alternatively, aggressive tumor biology may permit transient sensitivity followed by rapid progression. Differences in drug delivery, tumor microenvironment, or resistance mechanisms may also contribute. Clarifying this counterintuitive finding will require dedicated molecular and pharmacokinetic investigations.

Patients with central nervous system (CNS) involvement represented another clinically important subgroup. Although SG is not approved for the treatment of active brain metastases, accumulating observational evidence suggests that patients with treated or stable CNS disease may still benefit [17, 18]. In the present analysis, brain metastases were not associated with significantly worse PFS or OS. However, given the limited number of affected patients and the retrospective design, these results should be interpreted conservatively. Prospective studies are needed to better delineate the role of SG in CNS-involved disease.

The influence of prior immunotherapy exposure was also explored. A subset of patients—predominantly within the mTNBC group—had previously received immune checkpoint inhibitors (ICIs). In this cohort, prior ICI treatment did not appear to compromise outcomes following SG therapy. This observation is consistent with ASCENT trial data, which demonstrated preserved SG benefit regardless of earlier ICI exposure [13]. Emerging real-world studies further support SG use after immunotherapy [23, 27, 28], although prospective validation remains necessary.

Taken together, these subgroup analyses offer clinically meaningful insights into patient selection in real-world practice and emphasize the heterogeneity of treatment response. They also highlight the ongoing need for biomarker-driven approaches to refine SG use, particularly in heavily pretreated and biologically diverse patient populations.

Finally, the objective response rate observed in this study was 52.9%, including complete responses in 10.3% of patients. This exceeds response rates reported in previous real-world cohorts, such as an Italian study documenting an ORR of 33.3% [23] and a US-based analysis reporting 27.8% [19]. Such differences may reflect variability in baseline disease characteristics, prior treatment exposure, adherence, or supportive care strategies, including the high rate of G-CSF utilization observed in this cohort.

Safety and tolerability profile

In the present study, sacituzumab govitecan (SG) demonstrated good overall tolerability, with adverse events (AEs) aligning with those documented in pivotal clinical trials and previous real-world investigations. The most common AEs were alopecia (64.7%), anemia (52.9%), neutropenia (50%), and diarrhea (38.2%). Severe (grade ≥ 3) hematologic adverse events, particularly neutropenia, affected a considerable number of patients; however, these were effectively controlled through G-CSF support, which was used in 88.2% of cases. Treatment discontinuation secondary to AEs occurred in only 2.9% of patients, and no novel safety concerns were identified. These results corroborate the known safety profile of SG established in the ASCENT [13] and TROPiCS-02 [14] trials. Moreover, they are in agreement with data from additional real-world cohorts. For example, a multicenter Italian study identified anemia (66.6%), neutropenia (59.6%), and diarrhea (38.6%) as the predominant toxicities, with 5.3% of patients stopping treatment due to AEs [23]. Comparable toxicity patterns were also described in German [17] and Polish [16] patient series, indicating that SG-related adverse effects are largely foreseeable and amenable to supportive interventions.

A recently published meta-analysis reinforced these data, finding that while SG carries a greater risk of grade 3–4 neutropenia and anemia relative to conventional chemotherapy, it does not lead to a higher rate of treatment cessation [25].

Considering the extensive use of G-CSF in our patient population, the value of proactive supportive measures cannot be overstated. Timely detection and handling of hematologic toxicities play a key role in preserving dose intensity and reducing therapy delays. The results underscore the potential benefits of anticipatory approaches to prevent toxicity-driven interruptions in treatment.

Limitations

Several limitations should be acknowledged in this study, some stemming from contextual and regulatory circumstances unique to the research environment. Firstly, the retrospective nature of the analysis carries the risk of selection and information biases. Secondly, the modest cohort size restricted statistical power, especially in subgroup evaluations. Thirdly, biomarker assessments, including Trop-2 expression levels, were not performed, despite their possible prognostic or predictive relevance. Fourthly, variations existed across participating centers in terms of treatment decisions and supportive care protocols. Critically, the lack of a comparator arm prevents firm conclusions about SG efficacy. Consequently, the reported clinical outcomes should be viewed as descriptive rather than definitive proof of therapeutic benefit. Patient accrual was also constrained by reimbursement policies; at study commencement, SG was not covered by national health insurance for mHRPBC patients in Turkey. For mTNBC cases, coverage required at least two prior lines of chemotherapy in the metastatic setting. Such restrictions likely postponed SG initiation, narrowed patient access, lowered overall enrollment, and may impair the broader applicability of the results.

Clinical implications

In summary, this investigation offers real-world evidence regarding SG application in routine practice for individuals with metastatic triple-negative breast cancer (mTNBC) and metastatic hormone receptor-positive breast cancer (mHRPBC). Notably, it addresses a gap in real-world evidence for the mHRPBC population, adding meaningful insights to the current body of knowledge. Although observed progression-free survival (PFS) and overall survival (OS) outcomes resemble those from registration trials, the uncontrolled design demands prudent interpretation of treatment effects. The data indicate that SG is practicable in both molecular subtypes, even among extensively pretreated patients with endocrine resistance. Larger prospective trials incorporating control groups and biomarker guidance are needed to confirm these findings, refine patient selection criteria, determine optimal sequencing, and enhance supportive care practices.

Conclusion

This retrospective, multicenter real-world investigation offers descriptive evidence on the clinical outcomes and safety profile of sacituzumab govitecan (SG) in patients diagnosed with metastatic triple-negative breast cancer (mTNBC) or metastatic hormone receptor-positive breast cancer (mHRPBC). The results show that progression-free survival (PFS) and overall survival (OS) were largely comparable between the two molecular subtypes, indicating similar clinical courses in real-world settings during SG therapy.

Notably, the study fills an important evidence gap by presenting one of the earliest real-world experiences with SG in the mHRPBC cohort, which remains underexplored beyond randomized trials. Even after extensive prior endocrine treatments and several chemotherapy regimens, mHRPBC patients achieved outcomes akin to those in mTNBC, highlighting SG's possible utility in advanced, endocrine-refractory settings.

Key prognostic indicators, including ECOG performance status and liver metastases, emerged as important influencers of survival, emphasizing the role of initial patient characteristics in informing therapeutic choices. The safety profile aligned closely with data from pivotal trials, featuring controllable adverse events and minimal treatment cessations.

Overall, SG emerges as a practical treatment choice for both mTNBC and mHRPBC in everyday clinical practice. Additional prospective, comparator-inclusive trials incorporating biomarker stratification are needed to refine patient selection approaches, especially amid the changing therapeutic options for mHRPBC.

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