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Real-World Efficacy and Safety of Sacituzumab Govitecan in Pretreated Metastatic Triple-Negative and HR+/HER2− Breast Cancer: A Turkish Multicenter Cohort

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ABSTRACT

Sacituzumab govitecan (SG), an antibody-drug conjugate directed at Trop-2, has been approved for metastatic triple-negative breast cancer (mTNBC) and more recently for hormone receptor-positive/HER2-negative metastatic breast cancer (mHRPBC). Although its efficacy has been proven in controlled clinical trials, real-world insights—particularly those including both molecular subtypes—are still limited. This multicenter, retrospective investigation assessed real-world clinical effectiveness, tolerability, and prognostic determinants of SG therapy among patients diagnosed with mTNBC or mHRPBC. Sixty-eight individuals who received SG treatment between 2022 and 2025 at several oncology institutions across Turkey were included. Eligibility required at least one prior chemotherapy regimen for mTNBC and two prior lines, plus CDK4/6 inhibitors with hormone therapy, for mHRPBC. Outcomes assessed were progression-free survival (PFS), overall survival (OS), and objective response rate (ORR). Potential prognostic factors were examined through univariate and multivariate models. Adverse events (AEs) were documented and classified per NCI-CTCAE v5.0. Of the participants, 35 (51.5%) had mTNBC and 33 (48.5%) had mHRPBC. The median PFS was 6.1 months, and the median OS was 12.5 months, with no significant variation between groups. The overall response rate was 52.9%, with 10.3% achieving complete remission. Poorer outcomes for PFS and OS were independently linked to higher ECOG performance scores and hepatic metastases. Prior exposure to immunotherapy did not appear to lessen SG's effect. The treatment was largely well tolerated, most frequently causing alopecia, anemia, neutropenia, and diarrhea, with only 2.9% discontinuing due to toxicity. SG demonstrated comparable outcomes and manageable safety profiles across mTNBC and mHRPBC subgroups. Although PFS and OS findings were in line with those from clinical trials, the lack of a comparator arm restricts causal interpretation. Crucially, this work provides one of the earliest real-world datasets describing SG use in mHRPBC, underlining its clinical promise beyond trial conditions. These findings support SG as an effective therapeutic alternative for heavily pretreated patients and highlight the need for further prospective and biomarker-based studies.

Keywords: Sacituzumab govitecan, Real-world evidence, Metastatic breast cancer, Triple-negative subtype, Hormone receptor-positive subtype, Trop-2

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Introduction

Breast cancer continues to be the most prevalent malignancy among women globally. Despite advances in screening and treatment, it remains a leading cause of cancer-related death, particularly in advanced disease stages [1, 2].

Metastatic hormone receptor-positive, HER2-negative breast cancer (mHRPBC) represents about 70% of all breast cancers and is commonly managed with endocrine agents in combination with CDK 4/6 inhibitors. However, resistance to hormonal therapy eventually occurs, often requiring a shift to chemotherapy in later lines. In these settings, chemotherapy provides modest benefit and considerable toxicity, leading to reduced quality of life and a median OS of less than three years among endocrine-resistant cases [3-5].

Metastatic triple-negative breast cancer (mTNBC), representing 10-15% of all cases, progresses aggressively, with early visceral and CNS spread and high relapse rates. Due to the absence of targetable molecular markers, systemic chemotherapy remains standard, though with limited PFS and OS improvements [6, 7].

Sacituzumab govitecan (SG) is a novel antibody-drug conjugate that binds Trop-2, a transmembrane glycoprotein overexpressed in numerous epithelial malignancies, including both mTNBC and mHRPBC. SG combines a humanized anti-Trop-2 antibody with SN-38, the active metabolite of irinotecan, via a hydrolyzable linker, enabling selective cytotoxic drug release and a secondary "bystander" cytotoxic effect on nearby tumor cells [8-12].

After initial clinical success, SG received accelerated FDA approval in 2020 for patients with mTNBC after at least two prior treatments. Its efficacy was validated in the phase III ASCENT trial, which showed superior survival and response rates compared to standard chemotherapy [13]. Later, the TROPiCS-02 trial extended its indication to mHRPBC, confirming its advantage over physician-selected chemotherapy in endocrine-resistant populations [14].

Although controlled trials confirm its benefit, real-world data on SG use remain sparse, especially across both Trop-2-positive subtypes. Observational data can clarify its performance in routine practice, considering patient variability, treatment tolerability, and prognostic characteristics [15-19].

This multicenter, retrospective analysis aims to describe and compare real-world efficacy, safety, and predictors of response to SG in patients with mTNBC and mHRPBC. By examining both subgroups, the study provides a broader real-world understanding of outcomes and survival determinants in this patient population.

Materials and Methods

Study design and population

A retrospective analysis was carried out at several oncology institutions, covering a total of 68 female participants aged 18 years and older who were diagnosed with metastatic triple-negative breast cancer (mTNBC) or metastatic hormone receptor-positive breast cancer (mHRPBC). All patients had received treatment with sacituzumab govitecan (SG) during the years 2022-2025.

Women included in the mTNBC group had experienced disease progression following at least one chemotherapy or chemoimmunotherapy regimen. Those in the mHRPBC group were eligible if two or more chemotherapy lines had failed after prior exposure to CDK 4/6 inhibitors and other hormonal agents. Patients were not included if they had participated in an SG clinical trial, developed another primary malignancy in the previous five years (excluding localized, non-metastatic skin cancers), declined consent, or were male.

Because this investigation was retrospective and observational, with no comparison or control cohort, it was designed to document patient outcomes and tolerability under real-world clinical conditions rather than to determine therapeutic effectiveness.

Treatment approach

SG therapy was delivered intravenously at an initial dosage of 10 mg/kg on days 1 and 8 of every 21-day cycle. If a dose reduction became necessary, it was first adjusted to 7.5 mg/kg and, if further reduction was required, to 5 mg/kg, depending on patient tolerance. To lower the likelihood of neutropenia, most participants received granulocyte colony-stimulating factor (G-CSF) as preventive support. Treatment was continued until either disease advancement, intolerable adverse effects, or voluntary withdrawal occurred.

Study outcomes

Progression-free survival (PFS) and overall survival (OS) served as the principal outcomes. PFS referred to the time between the beginning of SG treatment and either disease progression or death, while OS was measured from the initiation of SG until death from any cause.

Safety analyses involved documenting all adverse events (AEs) according to their frequency and severity, using the National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 5.0. Records of dose reductions or permanent discontinuations related to toxicity were also kept.

Statistical evaluation

All statistical work was conducted using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Baseline demographic and clinical information was summarized descriptively. Continuous data were presented as means with standard deviations or medians with ranges, while categorical variables were shown as counts and percentages.

PFS and OS distributions were generated through the Kaplan-Meier method. Differences in survival across categories—such as molecular subtype (mTNBC vs. mHRPBC), ECOG performance status (PS 0 vs. PS 1), and metastatic location (liver, bone, brain, etc.)—were compared using the Mantel-Cox (log-rank) test.

Univariate analyses were performed to determine how baseline characteristics—including subtype, ECOG PS, metastatic sites, earlier therapies, and Ki-67 levels—affected survival. Variables with significant univariate results were entered into multivariate Cox regression models to identify independent prognostic factors, and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. Logistic regression was also used to find variables related to treatment response, incorporating predictors that reached significance in the univariate stage. All tests were two-tailed, and statistical significance was set at $p < 0.05$.

Ethical Approval

All participating institutions obtained ethics approval for this research. The main authorization was granted by the Istanbul Medipol University Ethics Committee (Decision No. 1209, dated 28 November 2024). Written informed consent was received from every participant before treatment began.

Results and Discussion

Baseline profile of participants

A summary of patient demographics and baseline characteristics is provided in **Table 1**. The median age of the 68 enrolled women was 48 years (range: 29-78). An ECOG PS of 0 was noted in 70.6% of the group. Previous exposure to taxane and anthracycline therapy was observed in 94.1% and 79.4% of patients, respectively. De novo metastatic disease was present in 26.5% of the cohort.

By subtype, 51.5% were classified as mTNBC, and 48.5% as mHRPBC. HER2 immunohistochemistry (IHC) 0 expression was found in 70.4% of individuals. Among metastatic cases, 42.6% had received up to three previous systemic therapy lines, whereas 55.9% had undergone more than three. The most common metastatic sites included lymph nodes (85.3%), bones (57.4%), and lungs (57.4%), followed by liver (51.5%) and brain (42.6%). Patients received a median of seven SG cycles (range: 3-37). G-CSF prophylaxis was administered in 88.2% of cases.

Table 1. Baseline characteristics.

Variable	Value
Age (median, range)	48 (29-78)
Newly diagnosed metastatic disease	18 (26.5%)
Molecular subtype	
mTNBC	35 (51.5%)
mHRPBC	33 (48.5%)
Her2 status	
Her2 0	52 (76.4%)
Her2 + 1	10 (14.7%)
Her2 + 2 (FISH negative)	6 (8.8%)
ECOG performance status	
0	48 (70.6%)
1	20 (29.4%)
Sites of metastasis	
Liver	35 (51.5%)
Lung	39 (57.4%)
Brain	29 (42.6%)
Bone	39 (57.4%)
Lymph node	58 (85.3%)
Previous immunotherapy exposure	22 (32.4%)

Dose reduction owing to adverse events	20 (29.4%)
Treatment cessation owing to adverse events	2 (2.9%)
Previous chemotherapy agents received	
Taxane	64 (94.1%)
Anthracycline	54 (79.4%)
Carboplatin	48 (70.6%)
Capecitabine	53 (77.9%)
Local therapy	60 (88.2%)
Prior treatment lines in metastatic setting	
≤3 lines	29 (42.6%)
>3 lines	38 (55.9%)
Number of sacituzumab govitecan cycles (median, range)	7 (3-37)
G-CSF administration with sacituzumab govitecan	60 (88.2%)

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

Clinical Outcomes

During a median observation period of 6.8 months (95% CI: 5.4-10.0), the study population demonstrated a median progression-free survival (PFS) of 6.1 months (95% CI: 4.83-7.43) and a median overall survival (mOS) of 12.5 months (95% CI: 9.92-15.07) **(Figures 1 and 2)**.

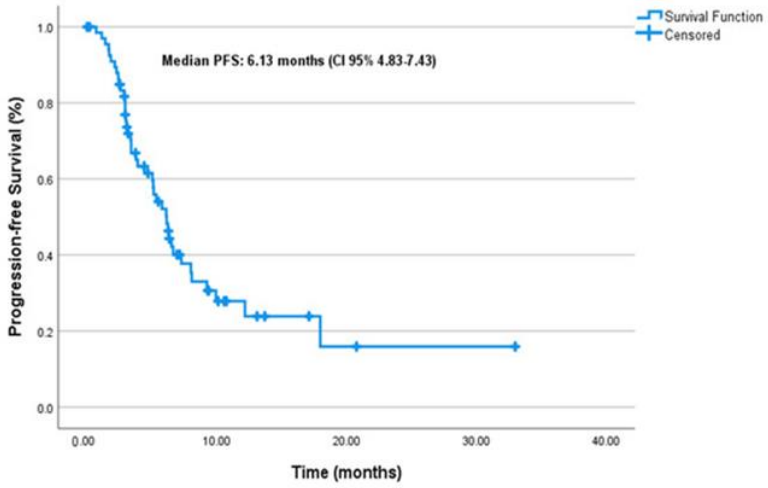

Figure 1. Progression-free survival.

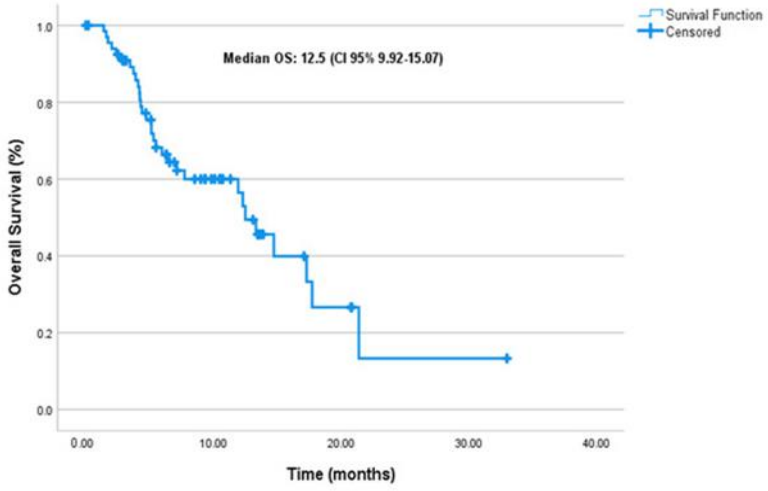

Figure 2. Overall survival.

Analysis by molecular classification revealed no significant variation in PFS between subtypes: 6.5 months for mTNBC and 5.76 months for mHRPBC (p = 0.78) **(Figure 3)**. Likewise, patients who initially presented with de novo metastatic disease showed no PFS difference (p = 0.63). However, performance status played a decisive role—patients with ECOG PS-0 had substantially longer PFS than those with ECOG PS-1 (p = 0.004).

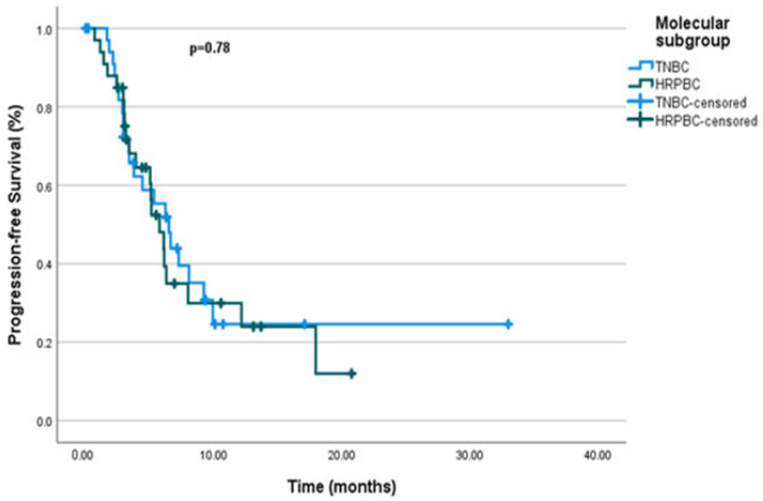

Figure 3. Progression-free survival according to molecular subgroup.

When considering metastatic distribution, liver involvement correlated with markedly shorter PFS (p = 0.002), and bone metastasis showed a similar negative association (p = 0.004). In contrast, lung (p = 0.088) and brain metastases (p = 0.253) were not statistically meaningful, nor was lymph node involvement (p = 0.086).

A history of prior immunotherapy failed to produce a significant difference (p = 0.886). Comparable results were seen across various chemotherapy regimens—including taxanes, anthracyclines, carboplatin, and capecitabine—none of which influenced PFS. Moreover, local treatment and the number of chemotherapy lines bore no significant relation to PFS.

In the analysis of Ki-67, patients with Ki-67 ≤ 20 versus > 20 exhibited no disparity in PFS (p = 0.897). Similarly, Ki-67 levels in metastatic samples did not relate to PFS outcomes. Dose reductions due to toxicity (p = 0.270) and G-CSF use (p = 0.097) also lacked statistical significance.

Overall, the findings highlighted ECOG PS, liver metastasis, and bone metastasis as major prognostic factors affecting PFS, whereas treatment regimen and Ki-67 status showed no measurable impact **(Table 2)**.

Table 2. Univariate and multivariate results for progression-free survival.

Variable	mPFS (Months)	95% CI	*p*-Value	HR (95% CI)	Multivariate *p*-Value
Molecular subgroup			0.78		0.348
mHRPBC	5.76	(4.28-7.24)		Ref.	
mTNBC	6.5	(4.45-8.54)		0.73 (0.384-1.401)	
De novo metastases					
Absent	6.13	(4.71-7.88)	0.63		
Present	5.13	(1.97-8.28)			
ECOG PS			**0.004**		**0.050**
ECOG PS-0	7.26	(5.32-9.21)		Ref.	
ECOG PS-1	3.76	(2.26-5.27)		1.96 (0.999-3.875)	
Liver metastases					
Absent	NR	(4.83-7.43)	**0.002**	Ref.	**0.047**
Present	4.43	(2.74-6.12)		2.04 (1.008-4.151)	
Lung metastases					
Absent	8.0	(6.19-9.80)	0.088		
Present	3.9	(2.30-7.76)			
Brain metastases			0.253		

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

mTNBC: metastatic triple-negative breast cancer; mHRPBC: metastatic hormone receptor-positive/HER2-negative breast cancer; ECOG PS: Eastern Cooperative Oncology Group performance status; G-CSF: granulocyte colony-stimulating factor; ICIs: immune checkpoint inhibitors; HR: hazard ratio; CI: confidence interval; NR: not reached; NA: not applicable; mPFS: median progression-free survival; Ref: reference.

In multivariate modeling, liver metastasis significantly increased the probability of disease progression (p = 0.047, HR = 2.046), and ECOG PS similarly predicted worse PFS (p = 0.050, HR = 1.968). Neither bone metastasis (p = 0.095) nor molecular subtype (p = 0.348) had a notable influence.

In the univariate OS analysis, molecular subtype also failed to produce a significant difference (p = 0.38): mTNBC demonstrated a median OS of 11.93 months (95% CI: 5.22-18.64), while mHRPBC reached 11.3 months (95% CI: 9.16-25.4) **(Figure 4)**.

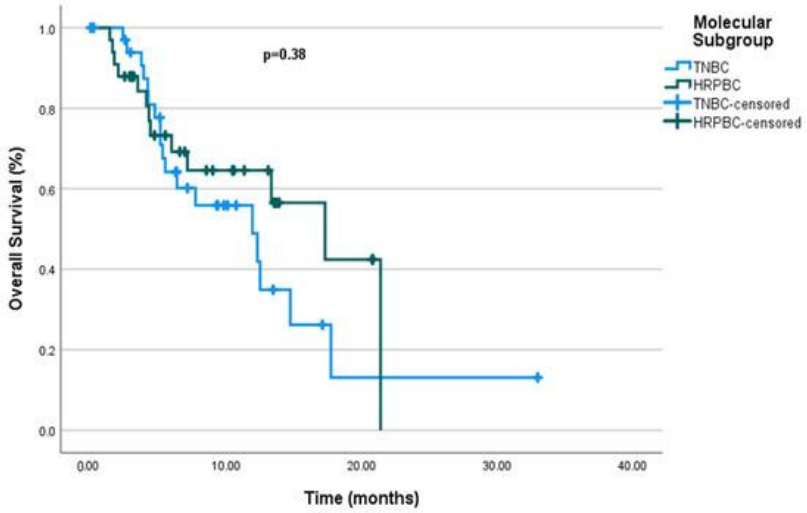

Figure 4. Overall survival by molecular subtype.

Among de novo metastatic cases, the median OS was 14.73 months (95% CI: 4.23-25.23), with no significant variance (p = 0.716). Similarly, ECOG PS was not associated with OS (p = 0.178).

Regarding metastatic involvement, liver metastasis was the strongest negative predictor of survival (median OS: 5.96 months, p = 0.001). Bone (11.93 months, p = 0.008) and brain metastases (7.13 months, p = 0.02) also corresponded to inferior outcomes, while lung metastasis did not reach significance (p = 0.076).

Among treatment modalities, carboplatin was linked with improved OS (12.30 months, p = 0.04), while anthracyclines and immunotherapy yielded no meaningful results (p > 0.05). Other clinical parameters—including number of chemotherapy lines, treatment discontinuation due to adverse effects, and G-CSF use—were also non-significant. Ki-67 expression, whether assessed at initial diagnosis or metastatic presentation, had no association with OS **(Table 3)**.

Table 3. Univariate and multivariate analyses for overall survival.

Variable	mOS (Months)	95% CI	*p*-Value	HR (95% CI)	Multivariate *p*-Value
Molecular subgroup			0.380		**0.046**
mHRPBC	11.30	(9.16-25.4)		Ref.	
mTNBC	11.93	(5.22-18.64)		0.46 (0.22-0.98)	
De novo metastases					
Absent	12.50	(10.78-14.21)	0.716		
Present	14.73	(4.23-25.23)			
ECOG-PS			0.178		
ECOG-0	14.73	(10.52-18.94)			
ECOG-1	13.33	(2.56-24.10)			
Liver metastases					
Absent	17.73	NA	**0.001**	Ref.	**0.022**
Present	5.96	(2.79-9.14)		3.15 (1.184-8.383)	
Lung metastases					
Absent	17.30	(11.29-23.31)	0.076		
Present	7.13	(3.65-14.78)			
Brain metastases					
Absent	17.30	(11.12-23.47)	**0.025**	Ref.	0.429
Present	7.13	(1.07-13.18)		1.39 (0.609-3.205)	
Bone metastases					
Absent	NR	NA	**0.008**	Ref.	0.073
Present	11.93	(4.98-18.88)		2.28 (0.927-5.624)	
Lymph node metastases			0.884		
Absent	21.40	NA			

Present	12.50	(10.72-14.27)	
Prior ICIs			
Absent	14.73	(4.89-24.57)	0.963
Present	12.50	(10.31-14.68)	
Prior chemotherapy			0.293
Taxane	-	-	
Antracycline	13.33	(4.56-22.10)	
Carboplatin	12.30	(4.71-19.88)	
Capecitabine	12.50	(9.95-15.04)	
Local treatment			
Absent	6.36	(0.10-16.03)	0.673
Present	12.50	(10.75-14.24)	
No. of chemotherapy lines			0.745
≤3 lines chemotherapy	14.73	(4.99-24.47)	
>3 lines chemotherapy	12.30	(5.81-18.79)	
Dose reduction due to toxicity			
Absent	12.50	(10.70-14.29)	1.00
Present	NR	NA	
G-CSF use with SG			
Absent	12.30	(0.10-24.75)	0.724
Present	13.33	(6.96-19.69)	
At diagnosis Ki-67			0.460
≤20%	14.73	(4.85-22.63)	
>20%	12.30	(6.02-18.57)	
Metastatic setting Ki-67			0.184
≤20%	14.73	(2.81-30.21)	
>20%	12.50	(10.82-14.17)	

Abbreviations are as in **Table 2**.

The multivariate OS assessment identified liver metastasis as an independent factor of poor prognosis (HR = 3.150, 95% CI: 1.184-8.383, p = 0.022). Bone metastasis approached significance (HR = 2.283, 95% CI: 0.927-5.624, p = 0.073). Molecular subtype remained relevant—mTNBC patients experienced better OS than those with mHRPBC (HR = 0.467, 95% CI: 0.221-0.987, p = 0.046). Brain metastasis lacked statistical effect (HR = 1.398, 95% CI: 0.609-3.205, p = 0.429).

Thus, liver metastasis and tumor subtype stood out as independent variables influencing OS **(Table 3)**.

Among 68 patients evaluable for response, the objective response rate (ORR) reached 52.9%, comprising 7 complete responses (10.3%) and 29 partial responses (42.6%). Additionally, 14.7% had stable disease, resulting in a disease control rate (DCR) of 67.6%.

Logistic regression revealed that liver metastasis (OR = 6.49, p = 0.038) and lung metastasis (OR = 7.59, p = 0.013) were both predictors of greater treatment responsiveness, increasing odds approximately 6.5- and 7.5-fold, respectively. Bone involvement showed a borderline relationship (OR = 4.35, p = 0.050). Conversely, lymph node metastasis corresponded with a reduced chance of response (OR = 0.065, p = 0.017). Other examined variables—including de novo metastasis, molecular subtype, ECOG PS, brain lesions, and Ki-67 index—did not demonstrate statistical significance (p > 0.05) (**Figure 5)**.

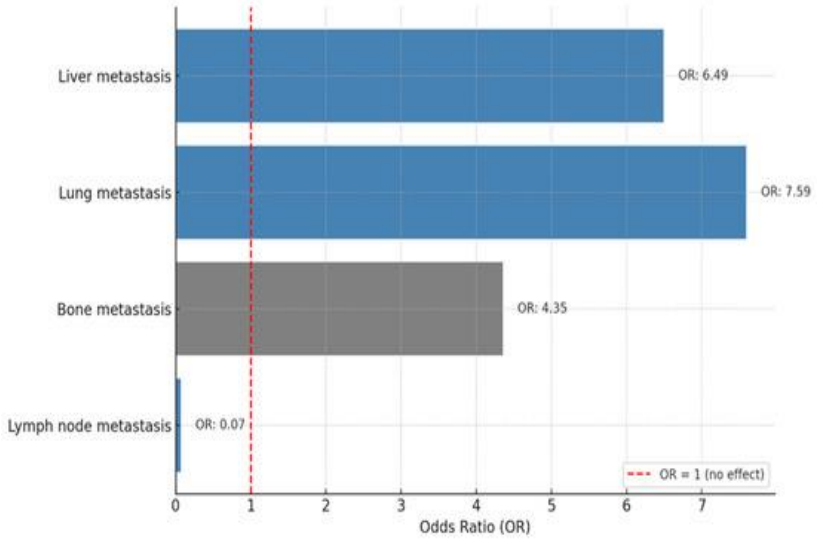

Figure 5. Predictive factors for treatment response.

Safety profile and adverse reactions

The adverse reaction overview is presented in **Figure 6**. The most prevalent side effect observed was hair loss, which affected 90% of participants. Anemia occurred in 41.7% of cases, with 15% progressing to grade ≥ 3 severity. Other common hematologic toxicities, including neutropenia and thrombocytopenia, frequently reached grade ≥ 3 intensity, underscoring the necessity for continuous blood count surveillance and supportive interventions. Prophylactic administration of granulocyte colony-stimulating factor (G-CSF) was employed in 88.2% of the study population to prevent or mitigate neutropenia, highlighting its essential role in minimizing SG-induced hematologic complications.

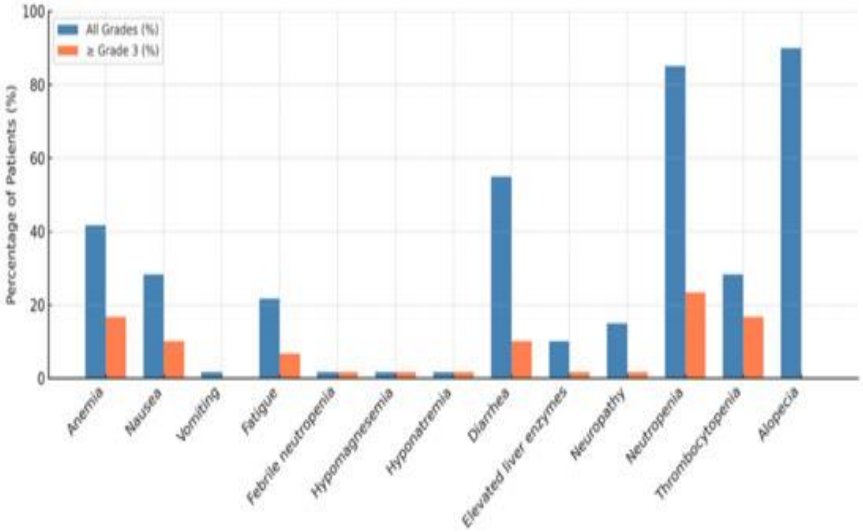

Figure 6. Overview of Reported Adverse Events

Among the non-blood-related toxicities, gastrointestinal issues such as nausea and diarrhea predominated. Patients presenting with grade 2 or higher nausea or vomiting typically received combination antiemetic therapy consisting of dexamethasone, serotonin (5-HT3) receptor blockers, and neurokinin-1 (NK-1) receptor inhibitors. Cases of grade 2 or higher diarrhea were managed using standard anti-diarrheal medications, reflecting an anticipatory strategy for managing gastrointestinal side effects. Fatigue was experienced by 21.7% of patients, though only a few developed higher-grade symptoms. Occurrences of elevated hepatic enzymes and febrile neutropenia were rare and did not necessitate treatment suspension.

Dose adjustments due to adverse effects were implemented in 29.4% of cases, while treatment cessation occurred in 2.9% of the cohort owing to therapy-resistant grade 4 thrombocytopenia. These observations emphasize the necessity of early toxicity recognition and prompt intervention to sustain therapy continuity and clinical benefit.

Comparison of real-world and trial-based findings

This multi-institutional, retrospective, real-world analysis describes the clinical trajectory and tolerability of SG therapy in patients with mTNBC and mHRPBC treated across centers in Turkey. Although the median PFS and OS recorded were comparable to those seen in pivotal clinical trials, they should be interpreted descriptively rather than as proof of efficacy. The results provide observational insights into SG's therapeutic behavior across two biologically distinct subtypes under everyday clinical conditions [20, 21].

In the analyzed group, the median PFS was 6.1 months and median OS 12.5 months, closely mirroring data from key trials. The ASCENT study, for instance, showed a median PFS of 5.6 months and OS of 12.1 months in previously treated mTNBC patients [13], while TROPiCS-02 demonstrated 5.5 and 14.4 months in mHRPBC [14]. Similarly, the EVER-132-002 trial, which focused on Asian populations, reported a median OS of 21.0 months for patients receiving SG [22]. Though outcomes appear parallel, the observational design and absence of a comparison group necessitate cautious interpretation.

A notable contribution of this study is the inclusion of mHRPBC patients, for whom real-world evidence remains extremely limited. To date, this appears to be the first observational study assessing SG simultaneously in mTNBC and mHRPBC cases. While trials such as TROPiCS-02 and EVER-132-002 have validated SG's efficacy in mHRPBC, few real-world analyses have addressed this subgroup, leaving a considerable gap in the literature [16, 23].

In our sample, 33 individuals (48.5%) had mHRPBC and had previously received CDK4/6 inhibitors in combination with endocrine therapy and two or more chemotherapy regimens. Within this subgroup, the median PFS and OS were both 6.1 and 12.5 months, consistent with TROPiCS-02 trial outcomes (median PFS 5.5 months, OS 14.4 months) [14]. These findings reinforce SG's clinical relevance among pretreated mHRPBC patients and demonstrate outcomes comparable to those in controlled trial settings.

The EVER-132-002 trial also reported positive tolerability and survival outcomes among Asian mHRPBC patients [22]. However, no prior real-world analysis has specifically documented detailed mHRPBC outcomes, making this investigation an important addition that offers practical insight for managing chemotherapy-exposed, endocrine-resistant populations.

Our analysis identified two principal prognostic indicators—ECOG performance status (PS) ≥ 1 and liver metastasis—both significantly linked to shorter PFS and OS. This aligns with prior observational and trial-based subgroup analyses associating poor baseline performance and visceral involvement with less favorable prognoses [24-26]. Patients with ECOG PS ≥ 1 exhibited markedly shorter OS, underscoring the influence of functional baseline status on survival.

Liver metastases, in particular, emerged as a consistent predictor of reduced survival, echoing results from the ASCENT trial and meta-analyses suggesting limited SG benefit in patients with hepatic involvement [25]. Supporting evidence also comes from Italian and Polish real-world studies showing that liver metastases correlate with poorer clinical outcomes [16, 23].

Interestingly, while liver and lung metastases were associated with inferior overall survival, they were also independently linked to higher objective response rates (ORR). This paradox may indicate an early tumor shrinkage phase prior to progression or more efficient drug distribution in highly vascularized organs. Alternatively, patients might initially respond but later experience disease acceleration due to aggressive tumor biology or emerging resistance. Further molecular and pharmacokinetic exploration is warranted to clarify this relationship.

Another distinct subgroup within our sample included patients presenting with central nervous system (CNS) metastases.

Although SG is not officially indicated for individuals with active brain lesions, growing observational evidence—including findings from this study—suggests that patients with previously managed or stabilized CNS disease may still experience therapeutic advantages from SG [17, 18]. In our dataset, the presence of brain metastases did not show a statistically significant correlation with poorer PFS or OS outcomes. However, these results should be viewed cautiously because of the study's observational design and the relatively small number of participants with

CNS involvement. Controlled clinical investigations are needed to clarify SG's potential role in this patient subgroup.

Beyond these findings, an additional point of clinical relevance concerns the history of prior immunotherapy exposure. A fraction of participants, mostly those in the mTNBC category, had undergone immune checkpoint inhibitor (ICI) therapy before beginning SG. In our population, prior exposure to ICIs was not linked to inferior results following SG treatment. This observation aligns with the ASCENT trial, which similarly found that earlier ICI use did not negatively influence SG efficacy [13]. Recent real-world analyses likewise indicate that SG remains a viable therapeutic option for patients who have already received immunotherapy [23, 27, 28]. Nevertheless, prospective evaluations are still required to more clearly determine the effect of ICI pretreatment on SG response.

Together, these subgroup evaluations offer additional precision for patient selection in practical settings and emphasize the importance of further biomarker-based stratification to determine which individuals gain the most benefit from SG—particularly among heavily pretreated and clinically varied groups.

The objective response rate (ORR) was 52.9%, with a complete response (CR) rate of 10.3%. These rates exceed those previously reported in real-world analyses, such as an Italian study with an ORR of 33.3% [23] and a U.S. study showing 27.8% [19]. Such differences may result from variations in baseline demographics, disease extent, treatment consistency, or supportive care practices—including the extensive use of G-CSF in this cohort.

Safety and tolerability profile

In this analysis, SG demonstrated an acceptable safety profile, comparable with outcomes from prior trials and observational reports. The most frequently recorded side effects were alopecia (64.7%), anemia (52.9%), neutropenia (50%), and diarrhea (38.2%). A notable share of participants experienced severe (grade ≥ 3) hematologic events, particularly neutropenia, but these were effectively managed through G-CSF support, administered to 88.2% of patients. Only 2.9% discontinued therapy due to toxicity, and no previously unreported adverse events were detected.

These safety outcomes are in line with the established toxicity profile from ASCENT [13] and TROPiCS-02 [14] clinical trials and are consistent with real-world results from other countries. For instance, a multicenter Italian study observed anemia (66.6%), neutropenia (59.6%), and diarrhea (38.6%) as the main side effects, with 5.3% discontinuing due to toxicity [23]. Comparable observations have been reported from Germany [17] and Poland [16], reinforcing that SG-related side effects are largely predictable and controllable with standard care.

A recent meta-analysis also supports these patterns, concluding that although SG use may increase grade 3-4 anemia and neutropenia compared with standard chemotherapy, it does not significantly raise discontinuation rates [25].

Given the high proportion of G-CSF use in our population, proactive monitoring and timely management of hematologic toxicity appear essential for preserving treatment continuity. These findings underscore the significance of preventive approaches to minimize therapy interruptions caused by treatment-related toxicity.

Study limitations

This investigation carries several constraints, partly related to local healthcare conditions and regulatory factors. First, its retrospective structure could introduce selection and reporting biases. Second, the limited cohort size restricts the strength of statistical analyses, particularly within subgroups. Third, biomarker information, including Trop-2 expression, was unavailable, preventing molecular-level interpretation. Fourth, differences in treatment delivery and supportive care between participating centers may have influenced outcomes. The lack of a control arm also limits any definitive efficacy comparisons, meaning that results should be viewed as descriptive rather than confirmatory.

Furthermore, the small study population was affected by restricted access to SG. At the time of study initiation, reimbursement policies in Turkey did not cover SG for mHRPBC, and for mTNBC, approval was limited to patients who had received at least two prior chemotherapy regimens for metastatic disease. These reimbursement barriers delayed treatment initiation, reduced eligibility, and ultimately limited case enrollment, thus narrowing the generalizability of the findings.

Clinical implications

Overall, this study offers real-world data describing SG therapy outcomes among mTNBC and mHRPBC patients treated under standard clinical conditions. It contributes valuable insight to an area where real-world evidence, particularly for mHRPBC, remains scarce. Although the PFS and OS results mirror those of major trials, interpretation should remain cautious in the absence of a comparator group. The findings suggest that SG may serve as an effective therapeutic option across both subtypes, especially for patients with extensive prior treatment or endocrine resistance. Future prospective and biomarker-guided studies are needed to confirm these patterns and to refine patient selection, treatment sequencing, and supportive care protocols.

Conclusion

This multicenter, retrospective, real-world analysis provides descriptive insight into SG's performance and safety in mTNBC and mHRPBC cases. The observed PFS and OS results were comparable between both subtypes, indicating similar clinical trajectories under SG therapy.

Significantly, the study helps fill a gap in existing evidence by presenting one of the earliest real-world datasets on SG use in mHRPBC, a subgroup with limited post-trial data. Despite prior endocrine therapy and multiple chemotherapy lines, mHRPBC patients showed comparable outcomes to those with mTNBC, supporting SG's utility in heavily pretreated, endocrine-resistant settings.

Key prognostic indicators—ECOG performance status and liver metastases—emerged as major determinants of survival, underscoring the role of baseline clinical condition in treatment planning. The safety outcomes aligned with previous research, revealing manageable toxicities and minimal discontinuation.

In summary, SG demonstrates feasibility and acceptable tolerability in both mTNBC and mHRPBC populations under real-world practice. Future controlled and biomarker-driven research will be essential to optimize patient selection and therapeutic sequencing in advanced breast cancer management.

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