Sacituzumab govitecan (SG) in patients with previously treated unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) within routine clinical practice in Spain (TROPSPAIN): interim analysis of a retrospective, observational, multicentre study.

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Background

Sacituzumab govitecan (SG) is approved in the US, EU, and many other countries globally for treating adult patients with mTNBC who have received two or more systemic therapies, including at least one of them for advanced disease.

The ASCENT clinical trial demonstrated a clinically meaningful benefit of SG over chemotherapy (1).

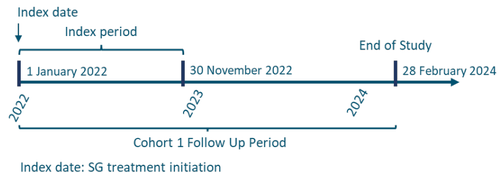
In Spain, SG was accessible through the Special Situation Medication program (MSE) from January 1, 2022 to November 30, 2022. Subsequently, from December 1, 2022, SG was included in the reimbursement system and became commercially available for mTNBC patients. Real world (RW) data on the utilization and outcomes of SG remain limited.

TROPSPAIN is a retrospective observational study to assess SG effectiveness and safety in a real-world setting in Spain.

Methods

- This is a RW study in mTNBC patients who initiated SG during MSE, (Cohort 1, January 1, 2022 – November 30, 2022) and commercial use (Cohort 2, December 1, 2022 – December 31, 2023).
- Primary objectives are to estimate RW overall survival (rwOS) and RW time to next treatment or death (rwTTNTD).
- Secondary objectives include a description of SG safety profile, demographic and disease characteristics, duration of SG treatment, and granulocyte colony-stimulating factor (G-CSF) comedication use.
- Stratified analysis of effectiveness outcomes by subgroups of interest included age (<65 vs ≥65 years old) and line of therapy with SG (2 vs ≥3).
- The results presented correspond to the interim analysis from cohort 1 patients (**Figure 1**).

Figure 1. Cohort 1 Study Design



1. **Bardía, A**. *et al*. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med 2021.

Results

Table 1. Patient characteristics		N=87
Female, N (%)		87 (100)
Age at mTNBC diagnosis (years), median (IQR)		49 (43-58)
De novo metastasis, N (%)		10 (11.5)
Age at SG treatment initiation (years), median (IQR)		51 (44-61)
SG line of treatment, N (%)	2	23 (26.4)
	3	21 (24.1)
	4+	43 (49.4)
Number of lines before SG, median (IQR)		2 (1-4)
Stage at SG initiation, N (%)	Unresectable/locally advanced	10 (11.5)
	Metastatic	77 (88.5)
Number of metastatic sites, N (%)	1	23 (26.4)
	2	26 (29.9)
	3	22 (25.3)
	≥4	6 (6.9)
	Missing	10 (11.5)
Metastatic sites, N (%)	Bone	37 (42.5)
	Brain	6 (6.9)
	Liver	21 (24.1)
	Lung	33 (37.9)
	Lymph nodes	41 (47.1)
	Other	22 (25.3)
	Missing	12 (13.8)
mTNBC HER2 expression*, N (%)	IHC 0	46 (52.9)
	IHC 1+	10 (11.5)
	IHC 2+/FISH-	13 (14.9)
	Missing	18 (20.7)
BRCA1/2 mutation status, N (%)	Mutated	4 (4.6)
	Wild type	30 (34.5)
	Missing	53 (60.9)
ECOG Performance Status, N (%)	0 -1	58 (66.7)
	2	8 (9.2)
	Missing	21 (24.1)
Patients' follow-up period (months), median (IQR)		9.2 (5.2 – 15.3)

*HER2 expression level on the most recent biopsy before SG initiation. HER2: Human epidermal growth factor receptor 2; FISH: Fluorescence *in situ* hybridization; IHC: Immunohistochemistry; IQR: Interquartile range. 2: second line; 3: third line; 4+: fourth line or later.

The interim analysis included 87 female patients from 18 Spanish sites who received SG during the MSE (cohort 1). Within the population, 11.5% were diagnosed with *de novo* metastasis. The median age at SG treatment initiation was 51 years, with 49.4% starting SG in fourth line or later; 66.7% of the patients had an ECOG performance status 0-1. Detailed patient characteristics are presented in **Table 1**.

Patients received SG for a median duration of 3.8 months (IQR 2.5 – 6.7). With a median follow-up of 9.2 months (IQR 5.2 – 15.3), the median rwOS was 9.3 months (**Figure 2a**) and the median rwTTNTD 4.5 months (**Figure 2b**). Treatment with SG in advanced lines of therapy in this population (49.4% in line 4+) may influence the observed OS and TTNTD.

Figure 2a. rwOS in patients with mTNBC treated with SG during the MSE

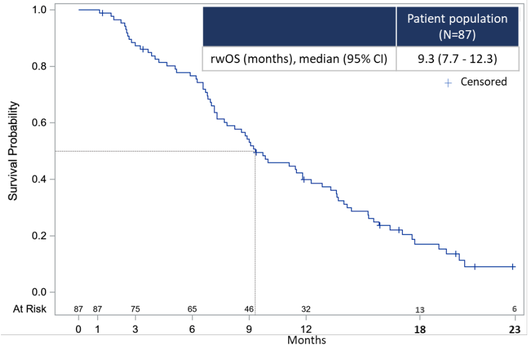
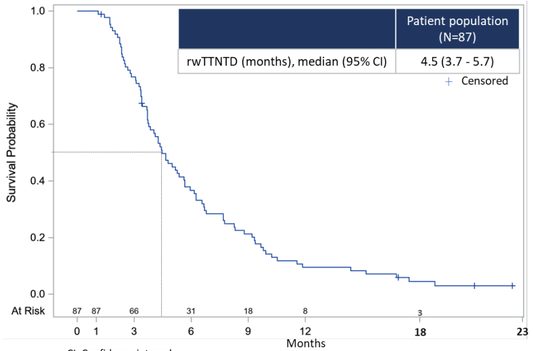


Figure 2b. rwTTNTD in patients with mTNBC treated with SG during the MSE



CI: Confidence interval.

The stratified analysis of rwOS and rwTTNTD by age and SG line of treatment are shown in **Table 2**. The mOS in younger patients and earlier line of SG use showed numerically better outcomes. Similarly, TTNTD are comparable between subgroups.

Table 2. Effectiveness outcomes by subgroup		N=87	Log-rank p-value
rwOS (months) by age (years), median (95% CI)	<65 (N=74)	10 (7.8-13.3)	0.3016
	≥65 (N=13)	7.7 (2.4-12.3)	
rwOS (months) by SG line of treatment, median (95% CI)	2 (N=23)	11.5 (6.8-14.2)	0.2954
	≥3 (N=64)	9 (7.2-12.3)	
rwTTNTD (months) by age (years), median (95% CI)	<65 (N=74)	4.5 (3.7-5.9)	0.8698
	≥65 (N=13)	5.3 (2.3-7.7)	
rwTTNTD (months) by SG line of treatment, median (95% CI)	2 (N=23)	5.7 (3.7-8.3)	0.1269
	≥3 (N=64)	4.3 (3.4-5.3)	

Table 3. Safety		
Patients with AEs, N (%)		75
Patients with AE resulting in treatment discontinuation, N (%)		1 (1.3)
Patients with AE resulting in treatment dose reduction, N (%)		24 (32)
Patients with AE resulting in treatment interruption, N (%)		26 (36.7)
Patients with Diarrhoea, N (%)		35 (46.7)
Patients with Neutropenia, N (%)		33 (44)
CTCAE grade of the AEs of interest reported		
Diarrhoea, N (%)	1	32 (57.1)
	2	19 (33.9)
	3	3 (5.4)
	Unknown	2 (3.6)
	Total	56
Neutropenia, N (%)	1	4 (7.4)
	2	19 (37.2)
	3	21 (41.2)
	4	7 (13.7)
	Total	51

AE: Adverse event. CTCAE: Common Terminology Criteria for Adverse Events.

Table 3 presents the safety profile on the study population. Adverse events (AEs) of any grade were reported in 75 (86.2%) patients. Among these patients, the AE resulted in SG discontinuation in 1 (1.3%) patient, in SG dose reduction in 24 (32%) patients, and in SG interruption in 26 (36.7%) patients. No treatment-related deaths were reported.

AEs of interest, diarrhoea and neutropenia of any grade, were reported in 46.7% and 44% of the patients, respectively. AEs were classified as grade 1 (mild) or 2 (moderate) in most of the cases (91% for diarrhoea and 44.6% for neutropenia).

Table 4 presents the use of concomitant G-CSF.

Table 4. G-CSF concomitant use	N = 33
Concomitant G-CSF primary prophylaxis, N (%)	14 (42.4)
Concomitant G-CSF secondary prophylaxis, N (%)	19 (57.6)

Study limitations

- The patient population under MSE tend to be heavily pretreated and have poor prognosis, who are not representative of the general mTNBC population. A younger population was observed compared to the ASCENT trial. Additionally, later line of SG use and poor ECOG may have contributed to slightly lower OS and TTNTD.
- The retrospective study design has limitations in capturing safety data. The lower rates compared to ASCENT may reflect underreporting of AEs due to incomplete medical charts.
- Results should be interpreted with caution due to the small sample size in the analysis.

Conclusions

- In this real-world study of the Spanish patients included in the MSE (cohort 1), 2L and later-line treatment with SG showed effectiveness and a manageable safety profile in mTNBC patients, comparable with the phase 3 ASCENT study (1) and other real-world evidence studies.
- Patients treated with SG had a median OS of 9.3 months and a median TTNTD of 4.5 months.
- The grade of the adverse events of interest, such as diarrhea and neutropenia, was 1 (mild) or 2 (moderate) in most of the cases.
- Patient data abstraction for cohort 2 in mTNBC patients treated with SG under commercial use is currently in progress at 20 Spanish sites, with results anticipated to be available at a future medical conference.

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