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Clinical features and drug-drug interactions of patients treated with Sacituzumab Govitecan for metastatic triple-negative breast cancer: a multicenter correlative real-world updated analysis

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Background

Sacituzumab Govitecan (SG), an antibody-drug conjugate (ADC) targeting TROP2, has demonstrated significant improvements in progression-free survival (PFS) and overall survival (OS) compared to standard chemotherapy in previously treated patients with metastatic triple-negative breast cancer (mTNBC). However, drug-drug interactions (DDIs), particularly in real-world settings, may influence the pharmacological activity of anticancer agents, potentially affecting both treatment efficacy and toxicity. Drug-PIN® (Personalized Interactions Network) is a tool designed to detect DDIs and integrate them with demographic, clinical, and biochemical patient data. In this multicenter retrospective analysis, we aim to evaluate the impact of clinical toxicities and DDIs on treatment outcomes in patients receiving SG in a real-world context.

Methods

Toxicities, drug-drug interactions (DDIs), and clinical outcomes - including PFS and OS - in patients with mTNBC treated with SG in routine clinical practice were retrospectively collected from 11 Italian centers, as part of the NCT02284581 multicenter study. DDIs were assessed using the Drug-PIN® platform, which generated a Drug-PIN® score and assigned each patient to a Drug-PIN® tier: green (no clinically significant DDIs), and yellow to red (increasing DDI severity). Patients with relevant DDIs (tiers yellow to red) were compared to those without significant interactions (tier green). PFS and OS were estimated using the Kaplan-Meier method. The association between Drug-PIN® classification and clinical outcomes was assessed through multivariate logistic regression.

References:
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Results

A total of 123 patients were included in the analysis. Median time from diagnosis of metastatic breast cancer (mBC) to SG start was 17 months (range 0- 115). Globally, 67 (54.5%) patients had at least one comorbidity, and 87 (70.7%) were receiving at least one concomitant medications. Among patients taking any medications, 20 patients (16.3%) had a relevant DDIs. Based on Drug-PIN score 102, 14, 5 and 2 patients were in the green, yellow, dark yellow and red tier, respectively. Baseline characteristics of patients are reported in table 1.

Table 1. Patient's characteristics.

Characteristics	Sacituzumab Govitecan N = 123
Age at SG start, year	
Median, years (range)	53 (26-78)
>60 years, no. (%)	36 (29.3)
≤60 years, no. (%)	87 (70.7)
Triple-negative breast cancer at initial diagnosis, n (%)	
Yes	98 (79.7)
No	25 (20.3)
Number of previous anticancer regimens for metastatic disease	
Median	2
Range	(0-7)
Time from diagnosis of MBC to SG initiation - months	
Median	17
Range	(0-115)
Number of metastatic site, n	
Median	3
Range	(1-6)
Major tumor locations, no. (%)	
Lung	61 (49.6)
Liver	40 (32.5)
Lymph nodes	77 (62.6)
Brain	33 (26.9)
Bone	61 (49.6)
Comorbidities, no. (%)	
0	56 (45.5)
1-2	56 (45.5)
≥3	11 (8.9)
Concomitant drugs, no. (%)	
0	36 (29.3)
1-2	46 (37.4)
3-5	30 (24.4)
≥6	11 (8.9)
Drug pin score	
Median	8.85
Range	(0-155)
Drug pin tier, no. (%)	
No concomitant drugs/Green	102 (82.9)
Yellow	14 (11.4)
Dark Yellow	5 (4.1)
Red	2 (1.6)

After a median follow-up of 15.2 months, 104 patients experienced disease progression and 80 died. The overall median rwPFS was 5.29 (95%CI: 3.98 - 6.97) and the overall rwOS was 11.6 months (95%CI: 8.9 - 14.7). Median rwPFS was 5.0 months in patients without any DDI and 2.8 months in patients with DDI [HR 1.89 (1.14-3.15) p.0.0138]. Using a multivariate model, both Drug-PIN tier [green vs other; HR 2.18 (1.3-3.5); p 0.0015] and presence of brain metastases at baseline [HR 1.62 (1.07-2.47) p 0.022] resulted as independent predictor of shorter PFS. Median OS was numerically higher but not statistically significant (p 0.098) in patients without DDIs [7.57 months vs 5.3 months [HR 1.69 (0.91-3.15)]. No significant association among DDIs and the report of common treatment related toxicity or dose reduction was detected. (Figure 1 and 2). The other efficacy results are reported in Table 2.

Figure 1. Kaplan Meier curve of Progression free survival according to Drug Pin tier.

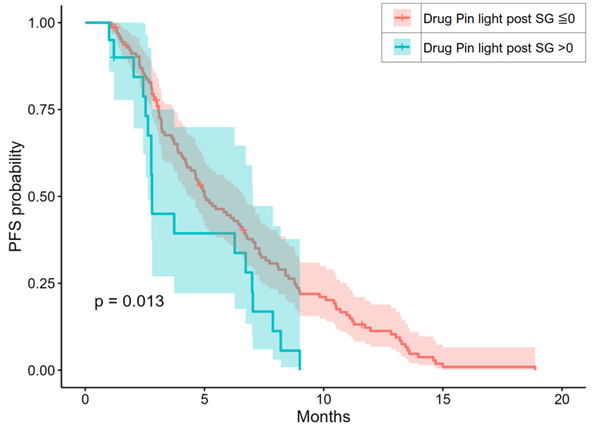


Figure 2. Kaplan Meier curve of Progression free survival according to SG dose.

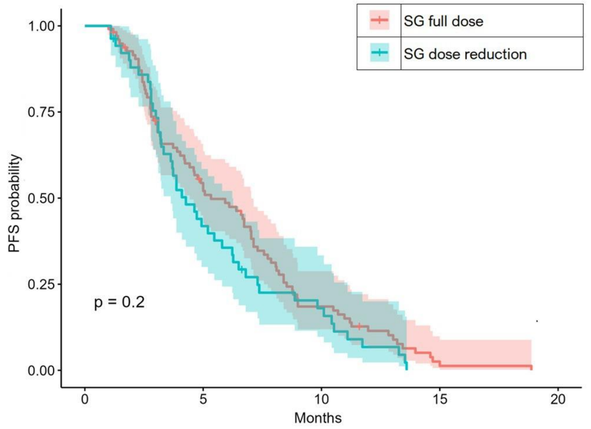


Table 2. Summary of treatment efficacy.

	Drug Pin light ≤ 0 N=102	Drug Pin light > 0 N = 21
Objective response – no. (%)		
Complete response	1 (0.9%)	0
Partial response	34 (33.4%)	8 (38.0%)
Stable disease – no. (%)		
no. of patients (%)	24 (23.6%)	7 (33.4%)
Progressive disease		
no. of patients (%)	41 (40.2%)	6 (28.6%)
Not evaluable		
no. of patients (%)	2 (1.9%)	0

Conclusion

In our real-world cohort, a low rate of clinically relevant DDIs was observed. While DDIs were associated with shorter PFS, no differences in toxicity or dose modifications emerged. Further investigations are needed to assess the potential impact of DDIs in mBC pts treated with ADCs.

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