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Effectiveness of sacituzumab govitecan in later-line treatment of mTNBC: real-world evidence from Poland, Czech Republic and Slovakia according to prior first-line pembrolizumab use

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BACKGROUND

- In the ASCENT trial, sacituzumab govitecan (SG) improved outcomes in metastatic triple-negative breast cancer (mTNBC), including those previously treated with programmed death-1 (PD-1) inhibitors, although results were numerically worse in this subgroup [1].
- As SG is used after progression on first-line chemoimmunotherapy with the PD-1 inhibitor pembrolizumab, concerns have arisen regarding its efficacy in this population.
- Several biological and clinical mechanisms could support the hypothesis that prior anti-PD-1 therapy may influence SG efficacy, including the selection of resistant clones, immune remodeling, functional decline, lack of mechanistic synergy, and acquired resistance to SN-38 [2,3].

AIM

- The purpose of this study was to evaluate the outcomes of SG according to prior use of pembrolizumab-based first-line treatment in Poland, the Czech Republic, and Slovakia.

MATERIALS AND METHODS

- A retrospective analysis of patients with mTNBC treated with SG was conducted across 18 oncology centers between August 2021 and May 2025.
- Patients were stratified according to prior exposure to first-line palliative chemoimmunotherapy with pembrolizumab.
- The assessed outcomes included progression-free survival (PFS), overall survival (OS), objective response rate (ORR), and disease control rate (DCR), with tumor response evaluated according to RECIST v1.1.
- Safety was analyzed based on adverse events (AEs) graded using CTCAE v5.0.
- Comparisons were performed using nonparametric and exact tests and survival analysis were conducted with univariate Cox models, with p<0.05 considered statistically significant.

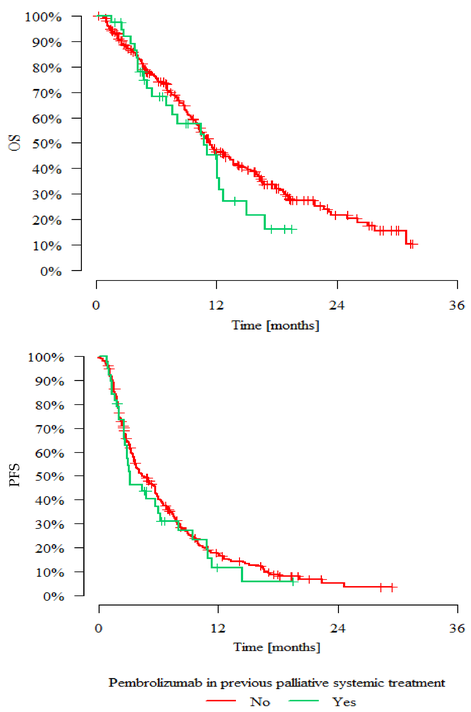


Figure 1. Kaplan–Meier curves for overall survival (OS), and progression-free survival (PFS) comparing patients previously treated and not treated with pembrolizumab.

RESULTS

- Of the 302 evaluated women, 38 (12.6%) had previously received first-line anti-PD-1-based therapy.
- No significant differences in demographic or disease-related characteristics were observed between the two subgroups, except for a lower frequency of germline *breast cancer gene 1 or 2* (*BRCA1/2)* mutations among patients previously treated with pembrolizumab (2.6% vs. 13.3%; p = 0.029).
- The median number of prior lines of palliative systemic therapy was 1 (IQR 1-2; range 1-7 in the anti-PD-1 group vs. 1-10 in the chemotherapy group; p=0.158).
- Brain metastases were present in 5/38 (13.2%) vs. 23/264 (8.7%) patients (p=0.372), and visceral metastases in 33/38 (86.8%) vs. 188/264 (71.2%) (p=0.066).
- A reduced starting dose of SG (≤8mg/kg) was administered in 2/38 patients (5.3%) previously treated with first-line anti-PD-1 therapy and in 25/264 (9.5%) of others (p=0.550).
- Median OS was 10.7 months in the anti-PD-1 group and 11.4 months in the chemotherapy group (HR=1.30; 95% CI: 0.836-2.021; p=0.244) (Fig.1).
- Median PFS was 3.2 vs.4.4 months, respectively (HR=1.14; 95% CI: 0.782-1.662; p=0.497) (Fig.1).
- The ORR was 28.9% (11/38) in the anti-PD-1 group vs. 31.1% (82/264) in the chemotherapy group (p=0.939), while DCR was 60.5% (23/38) vs. 64.8% (171/264) (p=0.742).
- Treatment-related toxicities were consistent with the established safety profile of SG, and no new safety signals were identified.

CONCLUSIONS

- SG maintained clinical benefit and safety profile irrespective of prior pembrolizumab exposure.
- Given the increasing use of perioperative pembrolizumab and the expected shift of SG to earlier treatment lines, the potential impact of prior immunotherapy on SG efficacy warrants further investigation across diverse mTNBC settings.
- Future studies should prospectively evaluate biological correlates of SG response following immune checkpoint inhibition, including TROP-2 expression, immune remodeling and genomic resistance mechanisms.

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Table 1. Efficacy and safety of SG by prior pembrolizumab treatment status.

PARAMETER		PEMBROLIZUMAB IN PREVIOUS PALLIATIVE SYSTEMIC TREATMENT NO (N=264)	PEMBROLIZUMAB IN PREVIOUS PALLIATIVE SYSTEMIC TREATMENT YES (N=38)	p
SG dose reduction due to AEs	No	165 (62.50%)	23 (60.53%)	0.956
	Yes	99 (37.50%)	15 (39.47%)	
SG administration delays due to AEs	No	97 (36.74%)	14 (36.84%)	1
	Yes	167 (63.26%)	24 (63.16%)	
Neutropenia grade 3 or 4	No	140 (53.03%)	25 (65.79%)	0.137
	Yes	124 (46.97%)	12 (31.58%)	
	Unknown	0 (0.00%)	1 (2.63%)	
G-CSF in primary prophylaxis for SG	No	181 (68.56%)	22 (57.89%)	0.261
	Yes	83 (31.44%)	16 (42.11%)	
Any G-CSF use	No	74 (28.03%)	11 (28.95%)	1
	Yes	190 (71.97%)	27 (71.05%)	
Number of full SG cycles	Mean (SD)	7.97 (6.84)	6.03 (4.7)	0.124
	Median (quartiles)	6 (3-11)	4 (2.25-9)	
	Range	0-41	1-19	
	n	262	38	
Number of SG administrations	Mean (SD)	16.2 (13.52)	12.26 (9.02)	0.117
	Median (quartiles)	13 (6-22)	7.5 (6-18)	
	Range	1-83	2-37	
	n	261	38	

Abbreviations: AEs, adverse events; ; G-CSF, granulocyte colony-stimulating factor; N, group size; n, cases of progression or death; p, univariate Cox proportional hazards model; SD, standard deviation; SG – sacituzumab govitecan.

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