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Real-World Outcomes with Sacituzumab Govitecan among triple-negative breast cancer patients with central nervous system metastases

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Background

Central nervous system (CNS) metastases, including brain metastases (BMs) and leptomeningeal disease (LMD) occur in approximately 20%-40% of patients (pts) with breast cancer during the course of their disease. Triple-negative breast cancer (TNBC) is associated with a high incidence (34%) of BMs and poor survival outcomes. Sacituzumab Govitecan (SG) has demonstrated significant improvements in progression-free survival (PFS) and overall survival (OS) in pre-treated pts with metastatic TNBC (mTNBC) in the pivotal ASCENT trial. However, data regarding SG efficacy in patients with TNBC and CNS metastases are limited, as 61 pts with stable/treated BMs were enrolled in the study and only 32 of them received treatment with SG. Patients with active BMs or LMD were excluded. This analysis aims to provide further insight into the clinical activity of SG in pts with mTNBC and CNS involvement.

Methods

Clinical and treatment data of pts with TNBC and BMs who were treated in a real-life setting, were retrospectively collected from 14 Italian cancer centers, as part of a multicenter, observational study (NCT02284581).
The objective of the present analysis was to evaluate the real-world activity of SG in pts with CNS metastases, both active or treated/stable, and LMD. CNS treatment response was retrospectively categorized as objective response, stable disease and progressive disease in the CNS. Overall real-world (rw)PFS and rwOS and CNS-specific progression free survival (CNS-PFS) were describing using the Kaplan-Meier method and reported with a 95% confidence interval. Survival outcomes between groups were compared by log-rank tests. Analysis was carried out with R software (version 4.5.1).

References:
1. Bardia A, et al. N Engl J Med. 2021;22(384):1529-1541.
2. Bardia A, et al. Journal of Clinical Oncology 2024;42(15):1738-1744
3. Caputo R, et al Front Oncol.2024;10.3389/fonc.2024.1362

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Results

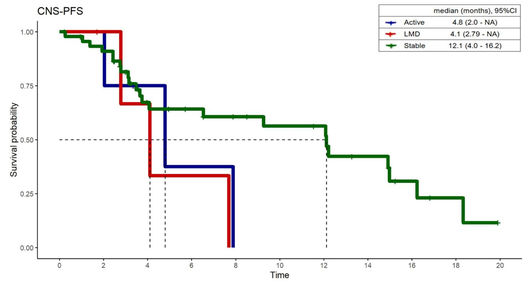
A total of 54 pts were included in the analysis. Of these 46 (85,2%) had treated/stable, 4 (7,4%) had active CNS metastases, and 4 (7,4%) LMD. The median age at SG initiation was 54 years (range 31-75). The median time from mTNBC diagnosis to CNS metastases was 12 months and the median time from CNS metastases diagnosis to SG initiation was 5 months. Pts had received a median of 2 previous lines of therapy before CNS involvement.
Baseline characteristics are reported in Table 1

Table 1. Clinicopathological characteristics of patients.

Characteristics	Sacituzumab Govitecan N = 54
Age, year	
Median	54
Range	31-75
ECOG performance-status score at screening, n (%)	
0-1	48 (94.2%)
2	3 (5.8%)
Germline BRCA1 or BRCA2 mutation status, n (%)	
Positive	11 (20.4%)
Negative/Unknown	43 (79.6%)
Triple-negative breast cancer at initial diagnosis, n (%)	
Yes	44 (81.5%)
No	10 (18.5%)
HER2-low breast cancer at initial diagnosis, n (%)	
Yes	12 (33.2%)
No	42 (77.8%)
Number of metastatic site, n	
Median	3
Range	(2-7)
Number of previous anticancer regimens for metastatic disease	
Median	3
Range	(0-5)
Number of Metastatic Lines prior to CNS metastases	
Median	2
Range	(0-4)
Previous use of PARP inhibitors — no. (%)	
Yes	10 (18.5%)
No	44 (81.5%)
Previous use of PD-1 or PD-L1 inhibitors — no. (%)	
Yes	16 (29.6%)
No	38 (70.4%)
Use of TDX-D post SG — no. (%)	
Yes	8 (17.0%)
No	39 (83.0%)
Prior surgery for CNS meatastases — no. (%)	
Yes	4 (10.3%)
No	35 (89.7%)
Prior radiation for CNS meatastases — no. (%)	
Yes	50 (92.6%)
No	4 (7.4%)
Type radiation for CNS meatastases — no. (%)	
WBRT	12 (24.0%)
SRS	38 (76.0%)

At a median follow-up of 18.2 months, the median overall rwPFS was 3.75 months (95% CI: 3.06 - 7.89 months) while rwOS was still immature. Median CNS-PFS in the overall population was 9.26 months (95%CI: 4.8 - 16.2), with subgroup medians of 12.1 months for stable/treated BMs, 4.8 months for active BMs, and 4.1 months for LMD. The CNS objective response rate (ORR) was 19.6% among pts with treated/stable BMs, and 25% in both pts with active BMs and those with LMD. Efficacy results are shown in figure 1 and table 2.

Figure 1. Kaplan Meier curve of Central Nervous System progression free survival (CNS-PFS).



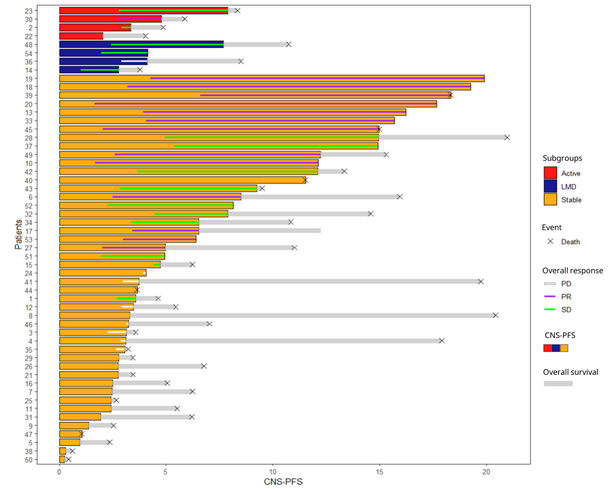
The CNS objective response rate (ORR) was 19.6% among pts with treated/stable BMs, and 25% in both pts with active BMs and those with LMD.

Table 2. Site of disease progression on SG

Respons to SG	Overall population N=54	Treated/Stable BM N= 45	Active BM N=4	LMD N=4
CNS response - n(%)				
Response (complete or partial)	11 (20.4%)	9 (19.6%)	1 (25%)	1(25%)
Stable disease	9 (16.6%)	7 (15.2%)	0	2 (50%)
Progressive disease	20 (37.0%)	16 (34.8%)	3 (75%)	1 (25%)
Not evaluable	14 (26.0%)	14 (30.4%)	0	0
Disease Control Rate	20 (48.8%)	16 (34.8%)	1 (25%)	3 (75%)
Clinical Benefit Rate at 6 months	8 (14.8%)	8 (17.4%)	0	0

Swimmers plot illustrating Central Nervous system progression free survival (CNS-PFS, colored line) and overall survival (OS, gray line), occurrence of extra-CNS progression and death in metastatic breast cancer patients with CNS metastases treated with Sacituzumab Govitecan.

Figure 2. Swimmers plot of CNS PFS and response from SG start according to stable/Active/LMD.



Conclusion

To our knowledge, this study represents the largest real-world analysis to date assessing the activity of SG in pts with TNBC and CNS metastases. Our findings are in line with the efficacy profile observed in the ASCENT trial, that did not include pts with active BMs and LMD. We report interesting preliminary data on CNS-ORR and CNS median-PFS.
These data support the potential role of SG in this difficult- to-treat population, although further studies are warranted to better characterize its activity in pts with mTNBC and CNS involvement.

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