Poster 198P

Relationship of Diarrhea and Neutropenia Events With Outcomes in Patients (Pts) With Metastatic Triple-Negative Breast Cancer (mTNBC) Treated With Sacituzumab Govitecan (SG): Post hoc Analysis From the Phase 3 ASCENT Study

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CONCLUSIONS

Clinical outcomes for pts with pretreated mTNBC with and without grade ≥ 3 neutropenia or grade ≥ 2 diarrhea were consistent with the overall population and were not adversely impacted by the occurrence of these AEs

OS for pts who experienced grade ≥ 2 diarrhea differed from those who did not experience diarrhea; however, in the time-varying Cox model, no significant difference was observed after adjusting for age, race, and BMI

Limitations included potential reporting bias from an open-label study and the post hoc nature of this analysis

Active monitoring and early intervention for neutropenia and diarrhea using established guidelines may allow for longer treatment durations and sustained benefit from SG

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BACKGROUND

- Pts with mTNBC have poor survival outcomes, and chemotherapy (CT) provides limited duration of response[1,2]
- SG, a first-in-class Trop-2–directed antibody-drug conjugate that carries SN-38 (the active metabolite of the topoisomerase inhibitor irinotecan) to tumor cells, is approved globally for mTNBC (following ≥ 2 prior CTs with ≥ 1 in the metastatic setting)[3]
- In the phase 3 ASCENT trial, SG significantly improved efficacy outcomes versus single-agent CT of physician's choice in pts with mTNBC treated in the second line (2L) or later.[4] Diarrhea and neutropenia were the most common adverse events (AEs) in this trial; these AEs can be effectively managed by following guidelines[3,4]

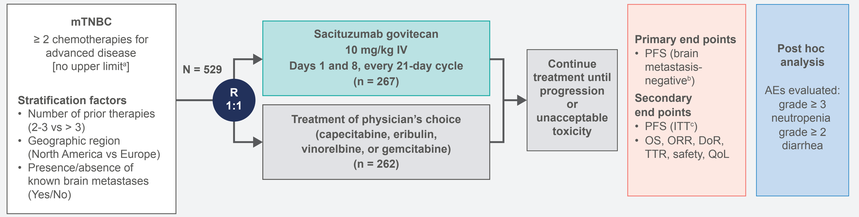
OBJECTIVE

- To study the relationship between neutropenia or diarrhea with clinical outcomes in patients with mTNBC who received SG in the ASCENT trial

METHODS

- Pts with mTNBC (per ASCO/CAP) who received SG in the phase 3 ASCENT study (NCT02574455) were included (**Figure 1**)
- A post hoc analysis was conducted to assess the relationship of neutropenia or diarrhea, separately, with progression-free survival (PFS) and overall survival (OS)
- This assessment focused on grade ≥ 3 neutropenia and grade ≥ 2 diarrhea as these events are generally considered most clinically relevant for SG
- A Cox regression was conducted, with a time-varying covariate having a value 0 before the onset of the first reported grade ≥ 2 diarrhea (grade ≥ 3 neutropenia) and a value 1 after the events were reported. For patients who did not experience grade ≥ 2 diarrhea (grade ≥ 3 neutropenia), the covariate value remained at 0 during the entire follow-up period
- The data cutoff for the analysis was February 25, 2021 (clinical database)

Figure 1. ASCENT study design and post hoc analysis



[a]1 of the required prior regimens could be from progression that occurred within a 12-month period after completion of (neo)adjuvant therapy.
[b]PFS measured by an independent, centralized, and blinded group of radiology experts who assessed tumor response using RECIST 1.1 criteria in patients without brain metastasis.
[c]The ITT population includes all randomized patients (with and without metastases). Baseline brain MRI only required for patients with known brain metastasis.
AE, adverse event; ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; DoR, duration of response; ITT, intent-to-treat; IV, intravenous; mTNBC, metastatic triple-negative breast cancer; MRI, magnetic resonance imaging; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QoL, quality of life; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; TTR, time to response.

Results

Table 1. Baseline characteristics, neutropenia[a]

	All patients (N = 258)	Grade ≥ 3 (n = 139)	No grade ≥ 3 (n = 119)
Age group, years, n (%)			
< 65	209 (81)	115 (83)	94 (79)
≥ 65	49 (19)	24 (17)	25 (21)
Race or ethnic group, n (%)			
White	211 (82)	112 (81)	99 (83)
Black	25 (10)	12 (9)	13 (11)
Asian	11 (4)	8 (6)	3 (3)
Other	11 (4)	7 (5)	4 (3)
Visceral metastases at baseline, n (%)	213 (83)	115 (83)	98 (82)
Median (min, max) time from metastases to first SG dose, months	17.9 (-0.1, 191.4)	18.2 (0.6, 191.4)	16.3 (-0.1, 88.2)
Median (min, max) number of prior systemic anticancer regimens	4 (2, 17)	4 (2, 17)	4 (2, 9)
Median (min, max) baseline BMI (kg/m²)	25.3 (15.0, 49.3)	26.0 (16.0, 49.3)	24.7 (15.0, 44.5)

[a]Neutropenia is defined as preferred term neutropenia, neutrophil count decreased, or febrile neutropenia.
BMI, body mass index; SG, sacituzumab govitecan.

Table 2. Baseline characteristics, diarrhea

	All patients (N = 258)	Grade ≥ 2 (n = 81)	No grade ≥ 2 (n = 177)
Age group, years, n (%)			
< 65	209 (81)	65 (80)	144 (81)
≥ 65	49 (19)	16 (20)	33 (19)
Race or ethnic group, n (%)			
White	211 (82)	68 (84)	143 (81)
Black	25 (10)	6 (8)	19 (11)
Asian	11 (4)	2 (3)	9 (5)
Other	11 (4)	5 (6)	6 (3)
Visceral metastases at baseline, n (%)	213 (83)	68 (84)	145 (82)
Median (min, max) time from metastases to first SG dose, months	17.9 (-0.1, 191.4)	19.5 (3.3, 98.8)	16.4 (-0.1, 191.4)
Median (min, max) number of prior systemic anticancer regimens	4 (2, 17)	4 (2, 17)	4 (2, 11)
Median (min, max) baseline BMI (kg/m²)	25.3 (15.0, 49.3)	27.7 (15.7, 49.3)	24.4 (15.0, 43.4)

BMI, body mass index; SG, sacituzumab govitecan.

Baseline characteristics and incidence of neutropenia and diarrhea

- For the SG-treated pts in this analysis, the incidence of grade ≥ 3 neutropenia was 54% (n = 139) and grade ≥ 2 diarrhea was 32% (n = 81)
- Baseline characteristics were generally similar among pts who experienced neutropenia or diarrhea (**Table 1** and **Table 2**); however, body mass index (BMI) was highest for patients who experienced grade ≥ 2 diarrhea
- There was only 1 discontinuation due to diarrhea (a nonserious grade 2 event); it was assessed as not related to study drug and was resolved
- There were no grade 5 events for either neutropenia or diarrhea

Treatment dose and intensity

- Treatment duration and relative dose intensity was generally similar for pts with and without grade ≥ 3 neutropenia (**Table 3**)
- Pts with grade ≥ 2 diarrhea had a longer duration of treatment (27.1 vs 17.4 weeks) and slightly lower dose intensity (97.7% vs 99.8%) than pts without diarrhea (**Table 3**)

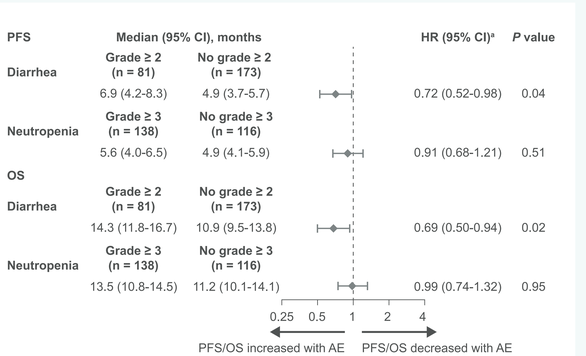
PFS and OS

- This post hoc analysis showed increased PFS and OS for pts with grade ≥ 2 diarrhea versus pts without diarrhea though these outcomes were consistent with the intent-to-treat population in both groups (**Figure 2**)
- Increased duration of therapy leading to higher cumulative AE risk may have confounded these results
- The differences in PFS and OS were not observed in the time-varying Cox model after adjustment for age, race, and BMI (**Figure 3**)
- PFS and OS were similar for patients with or without grade ≥ 3 neutropenia (**Figure 2** and **Figure 3**)

Table 3. Duration of treatment and relative dose intensity

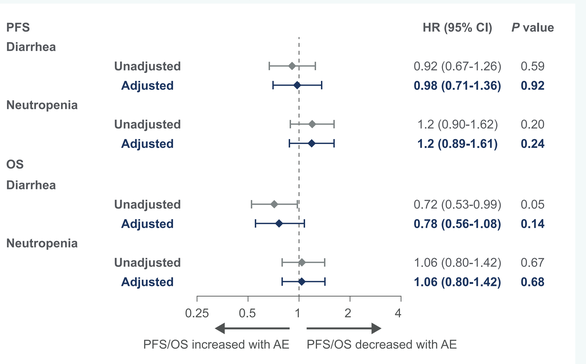
Neutropenia	All patients (N = 258)	Grade ≥ 3 (n = 139)	No grade ≥ 3 (n = 119)
Duration of treatment, weeks			
Median	19.1	21.9	18.0
(min, max)	(0.1, 128.6)	(0.1, 123.1)	(0.1, 128.6)
Relative dose intensity (%)			
Median	99.7	99.1	99.8
(min, max)	(53.7, 107.1)	(53.7, 107.1)	(59.8, 106.9)
Diarrhea	**All patients (N = 258)**	**Grade ≥ 2 (n = 81)**	**No grade ≥ 2 (n = 177)**
Duration of treatment, weeks			
Median	19.1	27.1	17.4
(min, max)	(0.1, 128.6)	(0.9, 128.6)	(0.1, 106.4)
Relative dose intensity (%)			
Median	99.7	97.7	99.8
(min, max)	(53.7, 107.1)	(53.7, 105.5)	(56.8, 107.1)

Figure 2. PFS and OS of pts with and without grade ≥ 3 neutropenia or grade ≥ 2 diarrhea



AE, adverse event; CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.
[a]Unstratified analysis.
Four pts died within 28 days after randomization and were excluded from this analysis.

Figure 3. Association between PFS, OS, and the onset of grade ≥ 3 neutropenia or grade ≥ 2 diarrhea after adjustment for age, race, and BMI



AE, adverse event; BMI, body mass index; CI, confidence interval; HR, hazard ratio; OS, overall survival; PFS, progression-free survival.
All 258 patients treated with SG in ASCENT were included in this analysis.

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DISCLOSURES

- Dr de Azambuja declares consultancy fees from AstraZeneca, Gilead, ImmunoPharma, Libbs, Lily, MSD, Nektar, Novartis, Odonate, Pierre Fabre, Roche/Genetech, SeaGen, Synthon, and Zodiac, and research grants from AstraZeneca, GSK, Novartis, Roche/Genetech, and Servier.