Assessment of Sacituzumab Govitecan in Black Patients From the Phase 3 ASCENT Study in Metastatic Triple-Negative Breast Cancer

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Background

Metastatic Triple-Negative Breast Cancer (mTNBC)

- mTNBC is a heterogenous disease with few treatment options and poor outcomes¹⁻³
- Single-agent chemotherapy remains standard for previously treated mTNBC, but is associated with low response rates and short progression-free survival (PFS)4-7
- TNBC is highly prevalent in Black women,⁸ with incidence rates twice as high compared with rates in White
- Black women with TNBC may experience worse clinical outcomes compared with non-Hispanic, White women with TNBC, including a higher risk of mortality potentially due to:8-9
- Disparities (eg, access to health care, delays in treatment, income)
- Comorbidities
- Differences in TNBC biology
- As a result, Black patients with TNBC may benefit from novel therapies to improve outcomes

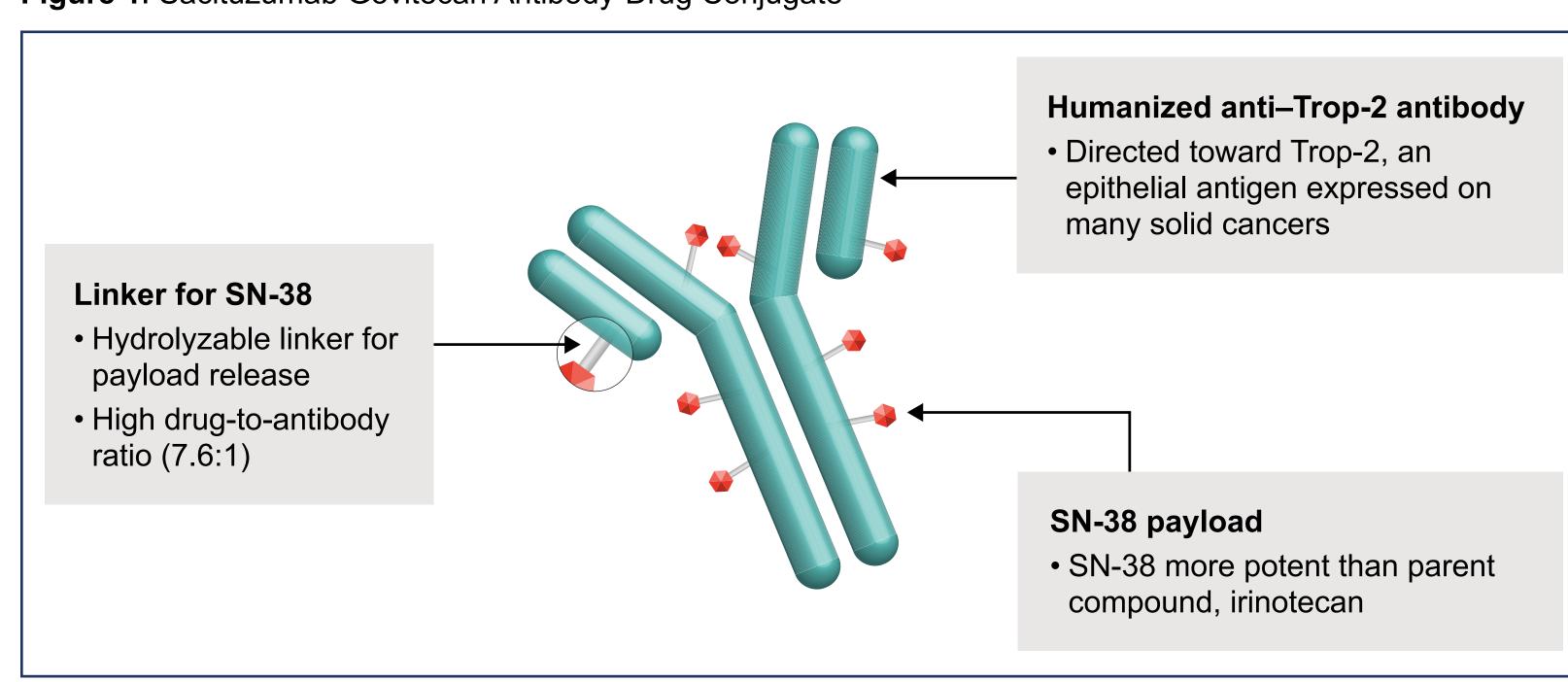
Sacituzumab Govitecan (SG)

- Trop-2 is expressed in all subtypes of breast cancer and linked to poor prognosis 11,12
- SG is an antibody-drug conjugate (ADC) composed of an anti-Trop-2 antibody coupled to the cytotoxic SN-38 payload via a proprietary, hydrolyzable linker¹³
- SG is distinct from other ADCs (Figure 1)¹³⁻¹⁷
- Antibody highly specific for Trop-2

greater (2L+) mTNBC setting¹⁷

- High drug-to-antibody ratio (7.6:1)
- Internalization and enzymatic cleavage by tumor cell not required for SN-38 (active metabolite of irinotecan) liberation from antibody
- Hydrolysis of the linker releases SN-38 extracellularly in the tumor microenvironment (bystander effect)
- The U.S. Food and Drug Administration (FDA) granted approval for SG for patients with mTNBC who received ≥2 prior chemotherapies (at least 1 in the metastatic setting) and FDA accelerated approval for patients with
- metastatic urothelial cancer who received platinum-containing chemotherapy and a checkpoint inhibitor^{16,18} • Results from the confirmatory phase 3 ASCENT study (NCT02574455) demonstrated a significant survival improvement of SG over single-agent chemotherapy, with a manageable safety profile in the second-line or
- Median PFS of 4.8 vs 1.7 months (HR, 0.43; 95% CI, 0.35-0.54) in the full trial population
- Median overall survival (OS) of 11.8 vs 6.9 months (HR, 0.51; 95% CI, 0.41-0.62) in the full trial population
- A prespecified subgroup analysis was performed to better understand the clinical outcomes of Black patients in the ASCENT study

Figure 1. Sacituzumab Govitecan Antibody-Drug Conjugate

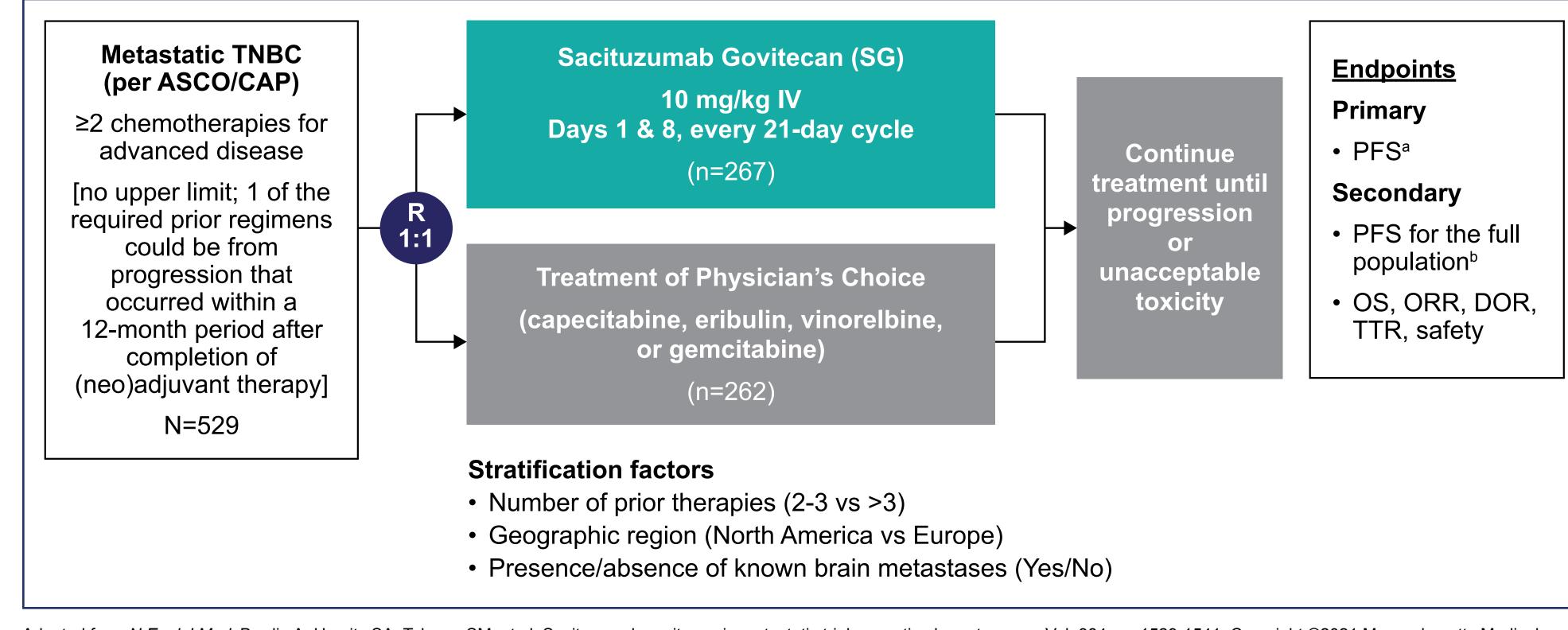


Methods

- In the phase 3 ASCENT trial, patients with mTNBC refractory to or relapsing after ≥2 prior chemotherapies (at least 1 in the metastatic setting) were randomized 1:1 to receive SG (10 mg/kg IV on days 1 and 8, every 21 days) or single-agent chemotherapy of physician's choice (TPC; capecitabine, eribulin, vinorelbine, or gemcitabine; Figure 2)¹⁷
- Primary endpoint was PFS per RECIST 1.1 by independent review in brain metastases-negative patients; key secondary endpoints included OS, objective response rate (ORR), clinical benefit rate (CBR), and safety Median PFS and ORR were assessed by blind independent central review (BICR) per RECIST 1.1
- In this post hoc subgroup analysis, efficacy outcomes were assessed in the full trial population of patients self-reporting Black race who were randomized to receive SG or TPC, including patients with and without known brain metastases
- Safety was analyzed in patients who received ≥1 dose of study drug in this subgroup
- Data cutoff was March 11, 2020

Methods (continued)

Figure 2. ASCENT: A Phase 3 Confirmatory Study of SG in Refractory/Relapsed mTNBC (NCT02574455)



Adapted from N Engl J Med. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. Vol. 384, pp 1529-1541. Copyright ©2021 Massachusetts Medical ^aPFS 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.

^bThe full population includes all randomized patients (with and without brain metastases). Baseline brain MRI only required for patients with known brain metastasis. ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; DOR, duration of response; IV, intravenous; mTNBC, metastatic triple-negative breast cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer; TPC, treatment of physician's choice; TTR, time to response. National Institutes of Health. https://clinicaltrials.gov/ct2/show/NCT02574455

Results

Patients

- A total of 529 patients were enrolled in the ASCENT trial (full trial population), of which 62 (12%) were Black patients (**Table 1**)

Of these patients, 28 were randomized to receive SG and 34 to receive TPC

- Baseline characteristics were generally balanced across treatment arms (**Table 1**)
- Two patients (3%; 1 each in the SG and TPC arms) were positive for BRCA1/2 mutations
- Six patients (18%) in the TPC arm had known brain metastases at study entry vs none in the SG arm
- Table 1. Demographics and Baseline Characteristics of ITT Population Reporting Black Race

Median treatment duration was 5.3 vs 1.6 months in the SG and TPC arms, respectively

	SG (n=28)	TPC (n=34)		
Female, n (%)	28 (100)	34 (100)		
Median age at study entry, y (range)	50 (35-69)	55 (32-75)		
ECOG performance status, n (%)				
0	12 (43)	14 (41)		
1	16 (57)	20 (59)		
Known brain metastases at study entry, n (%)	0	6 (18)		
TNBC at initial breast cancer diagnosis, n (%)	22 (79)	27 (79)		
Number of prior chemotherapies, n (%)				
2-3	21 (75)	22 (65)		
>3	7 (25)	12 (35)		
Median prior systemic regimens, ^a n (range)	4 (2-8)	4 (2-10)		
Previous use of checkpoint inhibitors, n (%)	11 (39)	12 (35)		
Setting of prior systemic therapies, n (%)				
Adjuvant	16 (57)	17 (50)		
Neoadjuvant	13 (46)	16 (47)		
Metastatic	25 (89)	34 (100)		
Locally advanced disease	2 (7)	0		
BRCA1/2 mutational status, n (%)				
Negative	13 (46)	17 (50)		
Positive	1 (4)	1 (3)		
Unknown	14 (50)	16 (47)		

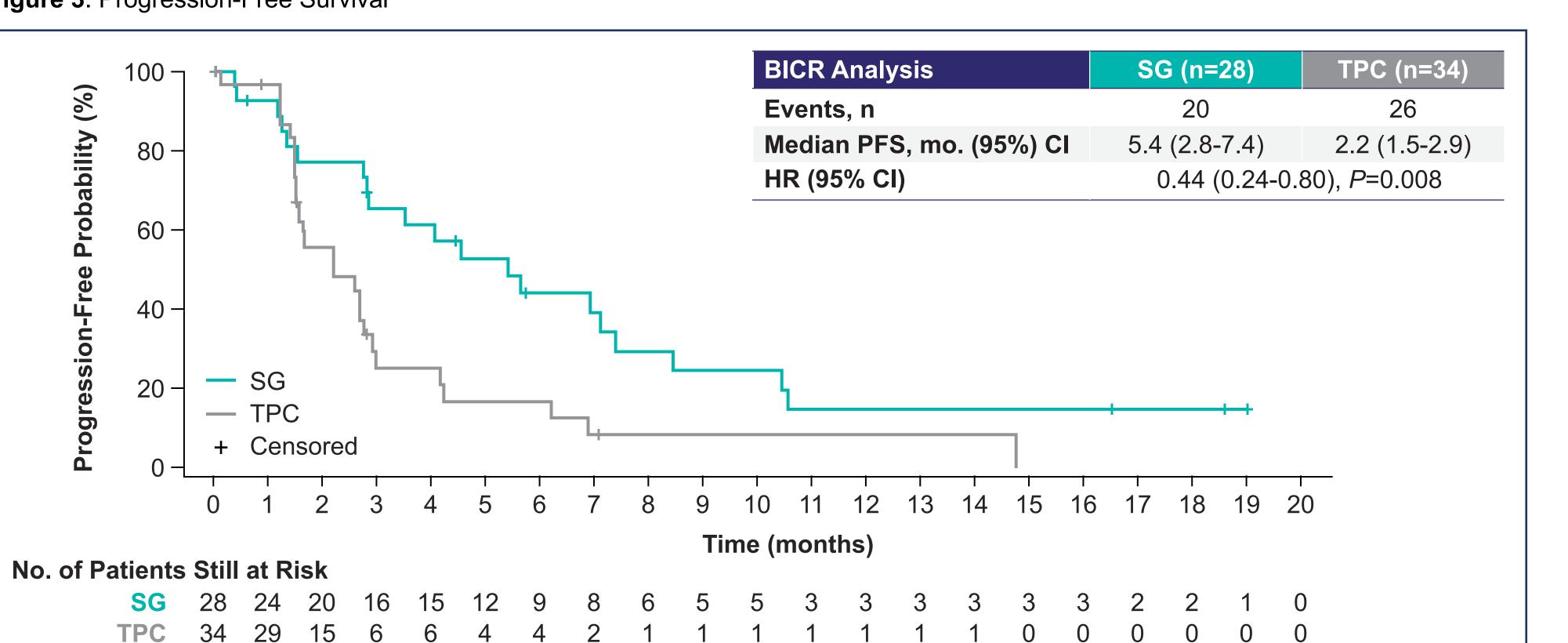
^aPrior systemic anti-cancer regimens are defined as regimens with a start and end date prior to first administration of study treatment BRCA, breast cancer gene; ECOG, Eastern Cooperative Oncology Group; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer; TPC, treatment of physician's choice; y, years.

Results (continued)

Efficacy in ITT Population Reporting Black Race

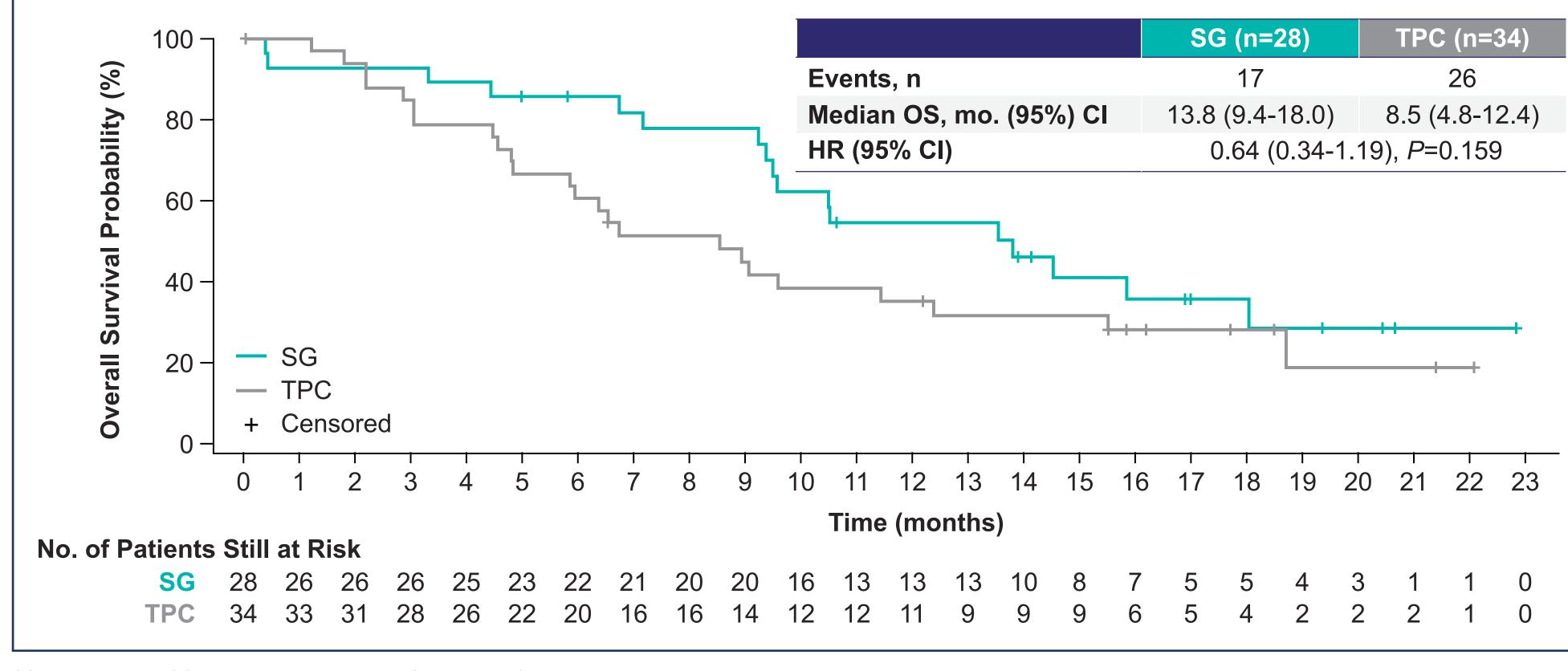
- Median PFS was improved with SG vs TPC (5.4 vs 2.2 months; HR, 0.44; 95% CI, 0.24-0.80; P=0.008; Figure 3) • Median OS was longer with SG vs TPC (13.8 vs 8.5 months; HR, 0.64; 95% CI, 0.34-1.19; *P*=0.159; **Figure 4**)
- ORR with SG vs TPC was 32% vs 6% (Table 2)
- In the SG arm, 1 patient (4%) had a complete response (CR) and 8 patients (29%) had a partial response (PR) In the TPC arm, 1 patient (3%) had a CR and 1 patient (3%) had a PR
- Median duration of response (DOR) was 9.2 months in the SG arm and not evaluable in the TPC arm (Table 2)
- Efficacy outcomes for SG in Black patients were consistent with those of SG in the full ASCENT study population 17

Figure 3. Progression-Free Survival



BICR, blinded independent central review; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Figure 4. Overall Survival



OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice

Table 2. Overall Response

SG, sacituzumab govitecan; TPC, treatment of physician's choice.

	SG (n=28)	TPC (n=34)		
ORR, n (%)	9 (32)	2 (6)		
Best overall response, n (%)				
CR	1 (4)	1 (3)		
PR	8 (29)	1 (3)		
SD	11 (39)	12 (35)		
SD >6 months	3 (11)	3 (9)		
PD	4 (14)	14 (41)		
Not evaluable	4 (14)	6 (18)		
CBR, ^a n (%)	12 (43)	5 (15)		
Median DOR, mo. (95% CI)	9.2 (3.2-NE)	NE (2.9-NE)		

BOR, best overall response; CBR, clinical benefit rate; CR, complete response; DOR, duration of response; NE, not evaluable; ORR, objective response rate; PR, partial response; SD, stable disease;

Safety in ITT Population Reporting Black Race

- The most common treatment-related adverse events (TRAEs; SG vs TPC) of any grade in this subgroup (Table 3) were neutropenia (64% vs 61%), diarrhea (64% vs 13%), and fatigue (52% vs 39%)
- The most common TRAEs (SG vs TPC) of grade ≥3 in this subgroup (**Table 3**) were neutropenia (48% vs 42%), anemia (12% vs 6%), leukopenia (8% vs 16%), and febrile neutropenia (8% vs 3%)

• The safety profile of SG in this subgroup was consistent with that of the full trial population¹⁷

- No SG-related events of severe cardiovascular toxicity, grade >1 neuropathy, or interstitial lung disease were reported in this subgroup
- Dose reductions due to treatment-emergent adverse events occurred in 28% vs 35% of patients in the SG vs TPC arms
- Discontinuations due to TRAEs occurred in 0% vs 3% of patients in the SG vs TPC arms
- No treatment-related deaths occurred in either arm

Table 3 TRAEs of Any Grade ($\geq 20\%$) and Grade ≥ 3 ($\geq 5\%$)

		SG (n=25)			TPC (n=31)		
TRAE		All grade, n (%)	Grade 3, n (%)	Grade 4, n (%)	All grade, n (%)	Grade 3, n (%)	Grade 4, n (%)
Hematologic	Neutropenia ^b	16 (64)	9 (36)	3 (12)	19 (61)	9 (29)	4 (13)
	Anemia ^c	10 (40)	3 (12)	0	9 (29)	2 (6)	0
	Leukopeniad	6 (24)	2 (8)	0	10 (32)	4 (13)	1 (3)
	Febrile neutropenia	2 (8)	2 (8)	0	1 (3)	0	1 (3)
Gastrointestinal	Nausea	11 (44)	0	1 (4)	11 (36)	0	0
	Diarrhea	16 (64)	1 (4)	0	4 (13)	0	0
	Vomiting	9 (36)	0	1 (4)	8 (26)	0	0
	Constipation	2 (8)	0	0	9 (29)	0	0
Other	Fatigue	13 (52)	0	0	12 (39)	3 (10)	0
	Alopecia	9 (36)	0	0	3 (10)	0	0

count decreased.' Combined preferred terms of 'anemia', 'hemoglobin decreased', and 'red blood cell count decreased'. Combined preferred terms of 'leukopenia' and 'white blood cell count decreased SG, sacituzumab govitecan; TPC, treatment of physician's choice; TRAE, treatment-related adverse events.

Conclusions

- In the phase 3 ASCENT study of SG in refractory/relapsed mTNBC, 12% of patients self-reported their race as Black
- Black patients treated with SG in the 2L+ mTNBC setting derived a similar clinical benefit from SG over TPC, consistent with that of the full trial population¹⁷
- Median PFS of 5.4 vs 2.2 months (HR, 0.44; 95% CI, 0.24-0.80; *P*=0.008) Median OS of 13.8 vs 8.5 months (HR, 0.64; 95% CI, 0.34-1.19; P=0.159)
- ORR of 32% vs 6%
- The safety profile of SG in Black patients from ASCENT was manageable, and consistent with that of the full trial population 17
- SG should be considered a treatment option for Black patients with mTNBC who have received ≥2 prior chemotherapies, with at least 1 in the metastatic setting

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Disclosures



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