Assessment of Sacituzumab Govitecan vs Treatment of Physician's Choice Cohort by Agent in the Phase 3 ASCENT Study of Patients With Metastatic Triple-Negative Breast Cancer

Poster 1077

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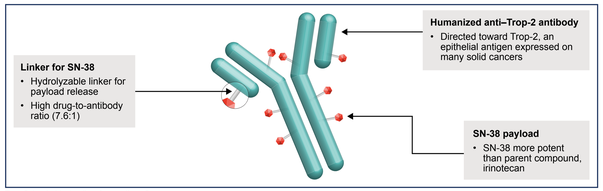
Background

- Metastatic triple-negative breast cancer (mTNBC) is a heterogenous disease with few treatment options and poor outcomes[1-3]
- Single-agent chemotherapy remains standard for previously treated mTNBC, but is associated with low response rates (<20%) and short median progression-free survival (PFS; 2-3 months)[4-9]
  - Eribulin is commonly used as monotherapy for previously treated mTNBC, but median PFS remains poor (<3 months)
- Sacituzumab govitecan (SG) is a novel antibody-drug conjugate (ADC) composed of an anti–Trop-2 antibody coupled to SN-38 via a proprietary hydrolyzable linker (**Figure 1**)
- SG is distinct from other ADCs[10-14]
  - Antibody highly specific for Trop-2
  - High drug-to-antibody ratio (7.6:1)
  - Internalization and enzymatic cleavage by tumor cell not required for SN-38 liberation from antibody
  - Hydrolysis of the linker releases SN-38 extracellularly in the tumor microenvironment (bystander effect)
- SG was granted FDA approval in April 2021 for patients with unresectable locally advanced or metastatic TNBC who have received ≥2 prior systemic therapies, at least one of them for metastatic disease based on results of the phase 3 ASCENT study[15]
- The pivotal ASCENT study demonstrated a significant survival improvement of SG over single-agent chemotherapy treatment of physician's choice (TPC), with a manageable safety profile in the second-line or greater mTNBC setting[16]
  - Median PFS of 5.6 vs 1.7 months (HR, 0.41; *P*<0.001)
  - Median overall survival (OS) of 12.1 vs 6.7 months (HR, 0.48; *P*<0.001)
- In this subanalysis from the ASCENT study, we assess safety and efficacy outcomes for SG vs each TPC agent to examine how each TPC agent performed individually

Figure 1. Sacituzumab Govitecan Antibody-Drug Conjugate

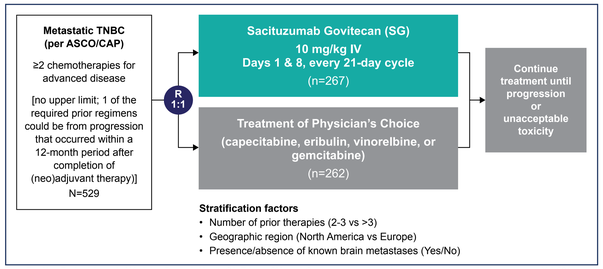


Trop-2, trophoblast cell surface antigen 2.

Methods

- ASCENT is a phase 3 trial of SG vs single-agent TPC, which included eribulin, vinorelbine, gemcitabine, or capecitabine (**Figure 2**)
- Efficacy outcomes were assessed in the brain metastases-negative (BMNeg) population for each agent
  - PFS (primary endpoint) and objective response rate (ORR) were assessed by blinded independent central review (BICR) per RECIST 1.1
  - Secondary endpoints were ORR per RECIST 1.1, duration of response (DOR), OS, and safety
- Safety outcomes were assessed in the population of patients who received ≥1 dose of study treatment (safety population) for each agent
- Data cutoff for analysis was March 11, 2020

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



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ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; IV, intravenous; TNBC, triple-negative breast cancer; R, randomization.

Results

Patients

- Of 529 total patients enrolled in ASCENT, there were 235 and 233 BMNeg patients in the SG and TPC arms, respectively
- Within the TPC arm, eribulin was the most commonly chosen chemotherapy (n=126), followed by vinorelbine (n=47), capecitabine (n=31), and gemcitabine (n=29)
- At data cutoff, 15 patients (6%) remained on treatment in the SG arm and no patients remained on treatment for any TPC agent (**Table 1**)
  - The most common reasons for treatment discontinuation for TPC agents were disease progression and withdrawal of consent
- Demographics and baseline characteristics for SG and each TPC agent subgroup were balanced between treatment arms (**Table 2**)

Table 1. Patient Disposition

	SG[a] (n=235)	TPC (n=233)[a]			
		Eribulin (n=126)	Vinorelbine (n=47)	Capecitabine (n=31)	Gemcitabine (n=29)
Randomized—no.	235	126	47	31	29
Randomized (not treated)—no. (%)	7 (3)	13 (10)	10 (21)	3 (10)	6 (21)
Remain on treatment—no. (%)	15 (6)	0	0	0	0
Discontinued treatment—no. (%)	213 (91)	113 (90)	37 (79)	28 (90)	23 (79)
Disease progression	199 (85)	95 (75)	29 (62)	23 (74)	19 (66)
Withdrawal of consent	4 (2)	12 (10)	6 (13)	2 (6)	3 (10)
Adverse event	6 (3)	0	3 (6)	2 (6)	2 (7)
Investigator decision	3 (1)	2 (2)	1 (2)	1 (3)	0
Death	1 (0.4)[b]	3 (2)	0	1 (3)	0
Treatment delay >3 weeks	0	2 (2)	0	0	0
Unacceptable toxicity	0	0	1 (2)	0	0

Assessed in the brain metastases-negative population.
[a]7 patients in the SG arm and 32 patients in the TPC arm were randomized but not treated in the brain metastases-negative population. [b]This was considered unlikely to be related to SG treatment.
SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Table 2. Demographics and Baseline Characteristics

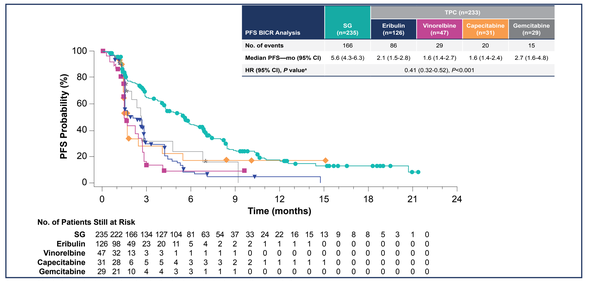
	SG (n=235)	TPC (n=233)			
		Eribulin (n=126)	Vinorelbine (n=47)	Capecitabine (n=31)	Gemcitabine (n=29)
Female—no. (%)	233 (99)	126 (100)	47 (100)	31 (100)	29 (100)
Median age (range)—y	54 (29-82)	53 (27-80)	54 (30-74)	50 (31-81)	56 (37-80)
Race or ethnic group—no. (%)					
White	188 (80)	98 (78)	35 (74)	25 (81)	23 (79)
Black	28 (12)	16 (13)	8 (17)	2 (6)	2 (7)
Asian	9 (4)	3 (2)	2 (4)	3 (10)	1 (3)
Other	10 (4)	9 (7)	2 (4)	1 (3)	3 (10)
ECOG performance score—no. (%)					
0	108 (46)	57 (45)	21 (45)	12 (39)	8 (28)
1	127 (54)	69 (55)	26 (55)	19 (61)	21 (72)
Number of prior chemotherapies from randomization stratification					
2-3	166 (71)	98 (78)	19 (40)	27 (87)	20 (69)
>3	69 (29)	28 (22)	28 (60)	4 (13)	9 (31)
Median prior anticancer regimens[a]—no. (range)	4 (2-17)	4 (2-14)	5 (2-14)	3 (2-7)	5 (2-9)

Assessed in the brain metastasis-negative population.
[a]Anticancer regimens refer to any treatment regimen that was used to treat breast cancer in any setting.
ECOG, Eastern Cooperative Oncology Group; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Efficacy

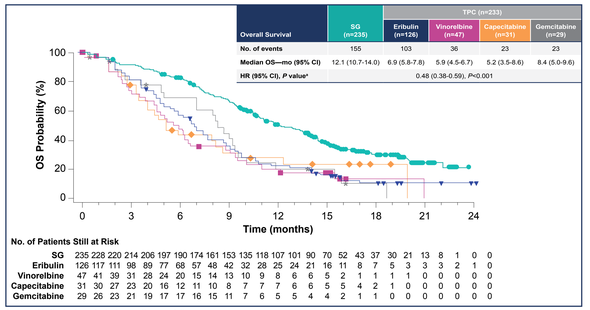
- Treatment with SG resulted in longer median PFS vs eribulin, vinorelbine, capecitabine, or gemcitabine (5.6 vs 2.1, 1.6, 1.6, or 2.7 months, respectively; **Figure 3**)
- Similarly, treatment with SG resulted in longer median OS vs eribulin, vinorelbine, capecitabine, or gemcitabine (12.1 vs 6.9, 5.9, 5.2, or 8.4 months, respectively; **Figure 4**)

Figure 3. Progression-Free Survival



Assessed by independent central review in the brain metastasis-negative population.
[a]Hazard ratio statistical analysis based on comparison of SG vs total TPC arm.
BICR, blinded independent central review; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Figure 4. Overall Survival



Assessed in the brain metastasis-negative population.
[a]Hazard ratio statistical analysis based on comparison of SG vs total TPC arm
OS, overall survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

- The ORR (35% vs 5%, 4%, 6%, or 3%), and clinical benefit rate (CBR; 45% vs 8%, 6%, 10%, or 14%) were higher with SG vs eribulin, vinorelbine, capecitabine, or gemcitabine, respectively (**Table 3**)
  - 10 patients in the SG arm had a complete response (CR) vs 2 patients in the TPC arm (eribulin)
- The median DOR was 6.3 months for SG and ranged from 2.8 to 3.6 months for TPC agents

Conclusions

- The efficacy benefit seen with SG vs TPC in patients with mTNBC in ASCENT was retained when evaluating each TPC chemotherapy agent individually (eribulin, vinorelbine, capecitabine, or gemcitabine)
  - Median PFS of 5.6 months vs 2.1, 1.6, 1.6, and 2.7 months
  - Median OS of 12.1 months vs 6.9, 5.9, 5.2, and 8.4 months
  - ORR of 35% vs 5%, 4%, 6%, and 3%
- SG has a manageable safety profile, with low rates of discontinuations due to AEs and no treatment-related deaths reported
- The safety profiles of eribulin, vinorelbine, capecitabine, and gemcitabine were consistent with that of TPC overall[16]
- These results confirm that SG should be considered as a new standard of care in patients with pretreated mTNBC

Table 3. Responses

	SG (n=235)	TPC (n=233)			
		Eribulin (n=126)	Vinorelbine (n=47)	Capecitabine (n=31)	Gemcitabine (n=29)
ORR—no. (%)	82 (35)	6 (5)	2 (4)	2 (6)	1 (3)
Best overall response—no. (%)					
CR	10 (4)	2 (2)	0	0	0
PR	72 (31)	4 (3)	2 (4)	2 (6)	1 (3)
CBR[a]—no. (%)	105 (45)	10 (8)	3 (6)	3 (10)	4 (14)
Median DOR—mo. (95% CI)	6.3 (5.5-9.0)	3.6 (2.9-4.2)	2.8 (NE)	NE	2.9 (NE)

Assessed by independent central review in the brain metastasis-negative population.
[a]CBR is defined as the percentage of patients with a confirmed best overall response of CR or PR and SD ≥6 months.
CBR, clinical benefit rate; CR, complete response; DOR, duration of response; NE, not evaluable; ORR, objective response rate; PR, partial response; SD, stable disease; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Safety

- Key grade ≥3 treatment-related adverse events (TRAEs) with SG vs eribulin included neutropenia (51% vs 31%), leukopenia (10% vs 5%), diarrhea (10% vs 0%), anemia (8% vs 2%), febrile neutropenia (6% vs 2%), fatigue (3% vs 5%), and peripheral neuropathy (0% vs 2%) (**Table 4**)
- Key grade ≥3 TRAEs with SG vs vinorelbine, capecitabine, and gemcitabine combined included neutropenia (51% vs 36%), leukopenia (10% vs 6%), diarrhea (10% vs 1%), anemia (8% vs 8%), febrile neutropenia (6% vs 2%), and fatigue (3% vs 6%), (**Table 4**)
- Discontinuation rates due to treatment-emergent adverse events for SG, eribulin, vinorelbine, capecitabine, and gemcitabine were 5%, 2%, 10%, 7%, and 9%, respectively
- 1 treatment-related death was reported for the TPC arm (eribulin; neutropenic sepsis) and none with SG

Table 4. TRAEs (All Grade, >20%; Grade 3/4, >5% of Patients)[a]

	SG (n=258)		TPC (n=224)			
			Eribulin (n=123)		Vin+Cap+Gem (n=101)	
TRAE[a]	**All grade, %**	**Grade 3/4, %**	**All grade, %**	**Grade 3/4, %**	**All grade, %**	**Grade 3/4, %**
Hematologic						
Neutropenia[b]	63	51	39	31	48	36
Anemia[b]	34	8	23	2	26	8
Leukopenia[b]	16	10	11	5	11	6
Febrile neutropenia	6	6	2	2	2	2
Gastrointestinal						
Diarrhea	59	10	8	0	17	1
Nausea	57	3	29	1	23	0
Vomiting	29	1	11	1	9	0
Other						
Alopecia	46	0	25	0	4	0
Fatigue	45	3	31	5	30	6

[a]Patients may report more than 1 event per preferred term. AEs were coded using MedDRA v22.1, and AE severity was graded per NCI CTCAE v4.03. [b]Neutropenia contains combined preferred terms of neutropenia and decreased neutrophil count, anemia contains combined preferred terms of anemia and decreased hemoglobin, and leukopenia contains combined preferred terms of leukopenia and decreased white blood cell count; all are counted once for each preferred term.
AEs, adverse events; cap, capecitabine; gem, gemcitabine; MedDRA, Medical Dictionary for Regulatory Activities; NCI CTCAE, National Cancer Institute Common Terminology for AE; SG, sacituzumab govitecan; TPC, treatment of physician's choice; TRAE, treatment-related AE; vin, vinorelbine.

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