Post-Progression Therapy Outcomes in Patients From the Phase 3 ASCENT Study of Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer

Poster P5-16-15d

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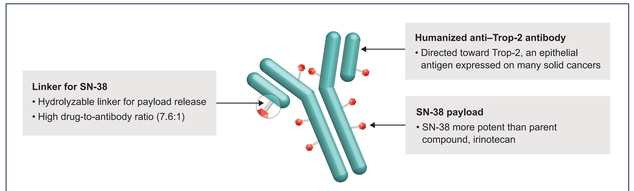
ASCENT Clinical Trial

Background

- Sacituzumab govitecan (SG) is a novel antibody-drug conjugate (ADC) composed of an anti-trophoblast cell surface antigen 2 (Trop-2) antibody coupled to SN-38 via a proprietary hydrolyzable linker (**Figure 1**)
- SG is distinct from other ADCs[1-5]
  - 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 (active metabolite of irinotecan) liberation from antibody
  - Hydrolysis of the linker releases SN-38 extracellularly in the tumor microenvironment (bystander effect)
- SG was granted U.S. Food and Drug Administration (FDA) approval for patients with metastatic triple-negative breast cancer (mTNBC) who received ≥2 prior chemotherapies (≥1 in the metastatic setting) and FDA accelerated approval for patients with metastatic urothelial cancer who received platinum-containing chemotherapy and a checkpoint inhibitor[6]
- Results from the confirmatory phase 3 ASCENT study demonstrated a significant survival improvement of SG over single-agent chemotherapy, with a manageable safety profile in the second-line or greater mTNBC setting[7]
  - Median progression-free survival (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
- Although sequential single-agent chemotherapy is the recommended approach following progressive disease (PD) on single-agent therapy for mTNBC, subsequent lines of therapy often result in poorer outcomes compared with earlier lines[8,9]
- In addition, outcomes and patterns of subsequent therapy for patients who discontinue SG following PD are not well characterized
- This *post hoc* subgroup analysis investigates post-progression treatment and OS of patients who discontinued SG due to PD during the ASCENT trial

Figure 1. Sacituzumab Govitecan Antibody-Drug Conjugate

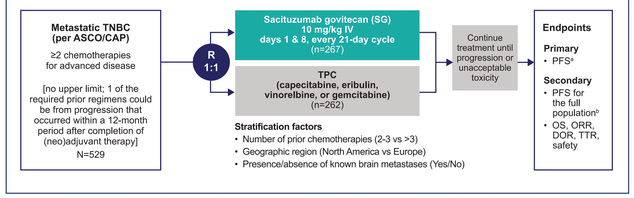


Trop-2, trophoblast cell surface antigen 2.

Methods

- In the phase 3 ASCENT trial, patients with mTNBC were randomized to receive SG or single-agent treatment of physician's choice (TPC; capecitabine, eribulin, vinorelbine, or gemcitabine) until disease progression or unacceptable toxicity (**Figure 2**)
- Primary endpoint was PFS per RECIST 1.1 by independent review in brain metastases-negative (BMNeg) patients; key secondary endpoints included PFS in the intent-to-treat (ITT) population, OS in the BMNeg and ITT populations, objective response rate, clinical benefit rate, and safety
- Post-progression outcomes were assessed in all patients with or without brain metastases who were randomized to receive SG and discontinued SG due to PD
  - Patients were followed every 4 weeks for survival and documentation of any further therapy for breast cancer
- Time to post-progression therapy was defined as the number of months from time of randomization until the initiation of subsequent anticancer therapy
- OS was analyzed in patients who did and did not receive post-progression therapy, and defined as the number of months from randomization or from end of SG treatment, using Kaplan-Meier estimates
  - OS HR and *P*-values were calculated using stratified log-rank test and stratified Cox regression, respectively
- Data cutoff was March 11, 2020

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



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[a] 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.
[b] The 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

- The ASCENT trial enrolled 529 patients, 267 (50%) of whom were randomized to receive SG
- Of 267 patients who were randomized to receive SG, 222 (83%) discontinued treatment due to PD
- Demographics and baseline characteristics at study entry of patients who did not receive post-progression therapy and those who received any post-progression therapy following SG were generally similar (**Table 1**)
  - Eastern Cooperative Oncology Group performance status (ECOG PS) was poorer in patients who did not receive post-progression therapy compared with those who received any post-progression therapy (ECOG PS 1, 69% vs 50%)
- Prior to SG discontinuation, these patients received SG for a median of 4.2 months (range, 0.0-18.7)
- Following SG discontinuation,163 of the 222 patients (73%) received post-progression therapy (**Table 2**)
  - Common post-SG therapies included eribulin (32%), carboplatin (15%), capecitabine (15%), and atezolizumab (7%)
  - Median time to receipt of post-progression therapy was 5.4 months (range, 1.0-19.8)

Table 1. Demographics and Baseline Characteristics

	Discontinued SG due to PD		
	Post-progression therapy (n=163)	No post-progression therapy (n=59)	All Patients (n=222)
Female, n (%)	162 (99)	58 (98)	220 (99)
Median age, y (range)	54 (30-82)	53 (27-80)	53 (27-82)
Race or ethnic group, n (%)			
White	133 (82)	49 (83)	182 (82)
Black	18 (11)	4 (7)	22 (10)
Asian	7 (4)	2 (3)	9 (4)
Other or not specified	5 (3)	4 (7)	9 (4)
Geographic region, n (%)			
North America	102 (63)	38 (64)	140 (63)
Rest of the world	61 (37)	21 (36)	82 (37)
ECOG performance status, n (%)			
0	81 (50)	18 (31)	99 (45)
1	82 (50)	41 (69)	123 (55)
Number of prior chemotherapies, n (%)			
2-3	114 (70)	37 (63)	151 (68)
>3	49 (30)	22 (37)	71 (32)
Median prior anticancer regimens,[a] (range)	4 (2-11)	4 (2-17)	4 (2-17)
Previous use of checkpoint inhibitors, n (%)	49 (30)	18 (31)	67 (30)
Setting of prior systemic therapies, n (%)			
Adjuvant	101 (62)	32 (54)	133 (60)
Neoadjuvant	78 (48)	31 (53)	109 (49)
Metastatic	157 (96)	58 (98)	215 (97)
Locally advanced disease	6 (4)	1 (2)	7 (3)
Known brain metastases at study entry, n (%)	18 (11)	5 (8)	23 (10)
TNBC at initial breast cancer diagnosis, n (%)	118 (72)	41 (69)	159 (72)
***BRCA1/2* mutational status, n (%)**			
Negative	90 (55)	37 (63)	127 (57)
Positive	14 (9)	2 (3)	16 (7)
Unknown	59 (36)	20 (34)	79 (36)

Assessed in the intent-to-treat population of patients randomized to receive SG, who discontinued treatment due to PD; data shown are at time of study entry.
[a] Prior 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; PD, progressive disease; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer.

Table 2. Most Common (>5%) Agents Received as Systemic Post-Progression Therapy

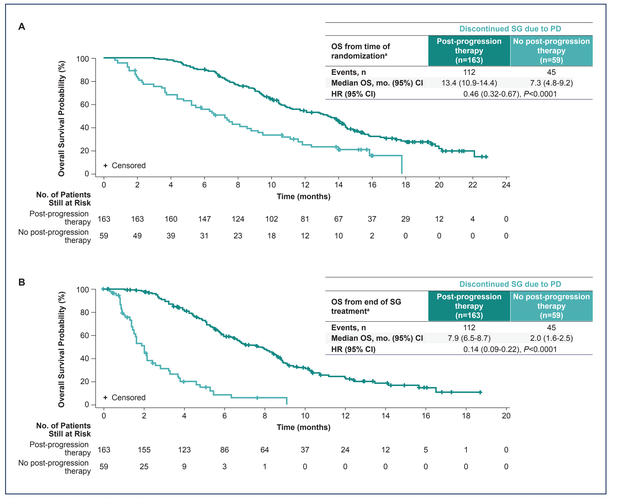
n (%)	Discontinued SG due to PD (n=222)
Any post-progression therapy[a]	163 (73)
Eribulin[b]	70 (32)
Carboplatin[c]	34 (15)
Capecitabine	34 (15)
Gemcitabine[d]	33 (15)
Vinorelbine[e]	21 (9)
Liposomal doxorubicin[f]	21 (9)
Paclitaxel	18 (8)
Atezolizumab[g]	15 (7)
Paclitaxel albumin	14 (6)

Assessed in the intent-to-treat population of patients randomized to receive SG, who discontinued treatment due to PD. Patients who have received more than one medication are counted once under each medication.
[a] WHO Drug Dictionary (WHODrug Global B3 201909) was used for coding. [b] Combined terms include the agents eribulin and eribulin mesilate. [c] Combined terms include the agents carboplatin and carboplatin; gemcitabine. [d] Combined terms include the agents gemcitabine, gemcitabine hydrochloride, carboplatin; gemcitabine, and cisplatin; gemcitabine hydrochloride. [e] Combined terms include the agents vinorelbine tartrate and vinorelbine. [f] Combined terms include the agents pegylated liposomal doxorubicin hydrochloride, liposomal doxorubicin hydrochloride, and pegylated liposomal doxorubicin. [g] Atezolizumab was received as monotherapy.
PD, progressive disease; SG, sacituzumab govitecan; TNBC, triple-negative breast cancer.

Overall Survival

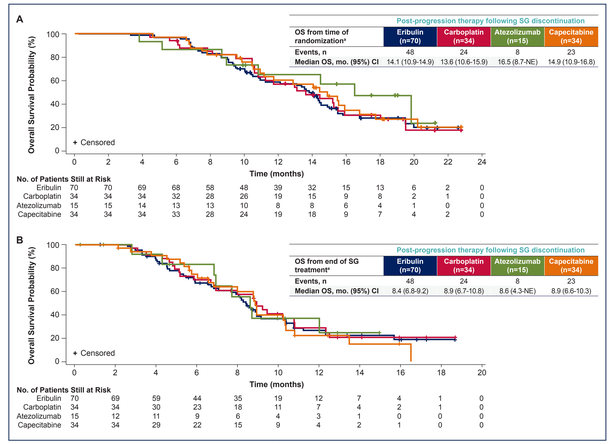
- Median OS was significantly longer in patients who received any post-progression therapy following SG compared with those who did not
  - Median OS from time of randomization: 13.4 vs 7.3 months (HR, 0.46; 95% CI, 0.32-0.67; *P*<0.0001; **Figure 3A**), respectively
  - Median OS from end of SG treatment: 7.9 vs 2.0 months (HR, 0.14; 95% CI, 0.09-0.22; *P*<0.0001; **Figure 3B**), respectively
- Median OS was similar in patients who received eribulin, carboplatin, atezolizumab, or capecitabine as post-progression therapy
  - Median OS from time of randomization: 14.1 (95% CI, 10.9-14.9), 13.6 (95% CI, 10.6-15.9), 16.5 (95% CI, 8.7 to not evaluable), and 14.9 months (95% CI, 10.9-16.8), respectively (**Figure 4A**)
  - Median OS from end of SG treatment: 8.4 (95% CI, 6.8-9.2), 8.9 (95% CI, 6.7-10.8), 8.6 (95% CI, 4.3 to not evaluable), and 8.9 months (95% CI, 6.6-10.3), respectively (**Figure 4B**)

Figure 3. Overall Survival by Receipt of Post-Progression Therapy



OS in patients who discontinued SG due to PD and received any post-progression therapy vs those who did not receive post-progression therapy, from time of randomization (A), and from end of SG treatment (B).
[a] Median OS was analyzed using Kaplan-Meier estimates, with HR and *P*-values calculated using stratified log-rank test and stratified Cox regression, respectively.
OS, overall survival; PD, progressive disease.

Figure 4. Overall Survival by Type of Post-Progression Therapy Received



Patients who received >1 post-progression therapy were included in the analysis of each therapy received.
OS in patients who discontinued SG due to PD and received eribulin, carboplatin, atezolizumab, or capecitabine as post-progression therapy, from time of randomization (A), and from end of SG treatment (B).
[a] Median OS was analyzed using Kaplan-Meier estimates.
NE, not evaluable; OS, overall survival; PD, progressive disease; SG, sacituzumab govitecan.

Conclusions

- In the ASCENT trial of patients with relapsed/refractory mTNBC, the majority (73%) of patients who discontinued SG due to PD were able to receive subsequent therapy post-progression
- A key difference in the baseline characteristics at study entry of patients who did not receive post-progression therapy following SG vs those who received any post-progression therapy was poorer ECOG PS (ECOG PS 1, 69% vs 50%)
- Common post-SG therapies included microtubule inhibitor (eribulin), platinum-based chemotherapy (carboplatin), checkpoint inhibitor (atezolizumab), and anti-metabolite (capecitabine) agents
- Patients who received post-progression therapy following SG had significantly improved median OS compared with those who did not receive further therapy
  - Median OS of 13.4 vs 7.3 months (HR, 0.46; *P*<0.0001) from time of randomization, respectively
  - Median OS of 7.9 vs 2.0 months (HR, 0.14; *P*<0.0001) from end of SG treatment, respectively
- Patients who received eribulin, carboplatin, atezolizumab, or capecitabine, as post-progression therapy following SG had similar median OS
- The results from this study indicate that treatment with SG does not prevent receipt of further systemic therapy for patients with relapsed/refractory mTNBC

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Disclosures

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