



Sacituzumab Govitecan Combined With Enfortumab Vedotin and Zimberelimab in Treatment-Naive Metastatic Urothelial Cancer: Interim Results From Phase 1b TROPHY-U-01 Cohort 7

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Declaration of Interests

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Background

- The treatment landscape for mUC is evolving rapidly, with EV + pembrolizumab as the preferred first-line regimen^{1,2}
 - EV + pembrolizumab demonstrated a median OS of 33.6 vs 15.9 months with platinum-based chemotherapy after 3.5 years of median follow-up
- In early datasets, SG, a Trop-2–targeting ADC, has shown encouraging activity as monotherapy and when combined with pembrolizumab or EV in pretreated patients with mUC³⁻⁵
 - In the phase 3 TROPiCS-04 study, SG monotherapy demonstrated an ORR of 23% (CR rate 5%) vs 14% (CR rate 3%) with chemotherapy although the primary endpoint of OS was not met
 - In the phase 1 DAD study, SG + EV demonstrated an ORR of 70%, including a CR rate of 13%
 - In Cohort 3 of the phase 2 TROPY-U-01 study, SG + pembrolizumab demonstrated an ORR of 41% (CR rate 20%) and manageable safety in patients who were pretreated with platinum therapy and were naïve to CPIs
- As EV and SG target distinct antigens (Nectin-4 and Trop-2) and deliver distinct cytotoxic payloads (MMAE and SN-38), they may provide complementary mechanisms of action alongside PD-1 inhibition⁶

TROPY-U-01 (NCT03547973) Cohort 7 evaluated SG + EV + the PD-1 inhibitor, zimberelimab, in participants with treatment-naïve mUC

ADC, antibody-drug conjugate; **CPI**, checkpoint inhibitor; **CR**, complete response; **EV**, enfortumab vedotin; **MMAE**, monomethyl auristatin E; **mUC**, metastatic urothelial cancer; **ORR**, objective response rate; **OS**, overall survival; **PD-1**, programmed cell death protein-1; **SG**, sacituzumab govitecan.
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TROPHY-U-01 Cohort 7: Study Design

Adults with histologically documented, previously untreated, locally advanced unresectable or metastatic urothelial cancer:

- Measurable disease by CT/MRI per RECIST 1.1
- Archival tumor tissue or fresh biopsy
- No prior systemic therapy for locally advanced or metastatic UC (curative therapy allowed if recurrence occurred > 12 months since last systemic treatment)
- ECOG performance status 0-1

**SG^a +
EV^b + ZIM^c**
Safety lead-in
Planned N = 12 to 36

**SG (7.5 mg/kg) +
EV^b + ZIM^c**
Stage 1 expansion
Planned N = up to 20

End points

Primary

- Safety and tolerability
- Confirmed ORR (INV, RECIST 1.1)

Secondary^d

- DOR, CBR, and PFS (INV, RECIST 1.1)
- OS

- DLTs were SG-related toxicities in safety lead-in participants who completed all cycle 1 dosing and 21-day evaluation period
- Primary granulocyte colony stimulating factor prophylaxis from cycle 1 was mandatory during each cycle unless clinically contraindicated per investigator
- At data snapshot (July 24, 2026), 21 participants (safety lead-in n = 13, expansion n = 8) were enrolled; median follow-up was 12.2 months
- SG 7.5 mg/kg was used for expansion

^aSG 7.5 mg/kg administered on days 1 and 8 of a 21-day cycle (SG 7.5 mg/kg was planned for safety lead-in; based on the incidence of DLTs, 5 mg/kg and 10 mg/kg doses could be evaluated). ^bEV doses of 1.25 mg/kg are administered on days 1 and 8 of a 21-day cycle. ^cZIM doses of 360 mg are administered on day 1 of a 21-day cycle. ^dEfficacy results in this presentation are based on INV; BICR- and iRECIST-related analyses are not included.

BICR, blinded independent central review; **CBR**, clinical benefit rate; **CT**, computed tomography; **DLT**, dose-limiting toxicity; **DOR**, duration of response; **ECOG**, Eastern Cooperative Oncology Group; **EV**, enfortumab vedotin; **INV**, investigator assessment; **iRECIST**, modified RECIST 1.1 for immune-based therapeutics; **MRI**, magnetic resonance imaging; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **RECIST**, Response Evaluation Criteria in Solid Tumors; **SG**, sacituzumab govitecan; **UC**, urothelial cancer; **ZIM**, zimberelimab.

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Demographics and Baseline Characteristics

	Cohort 7 (N = 21) ^a
Male, n (%)	16 (76)
Median age (range), yr	67 (39-83)
≥ 65 yr, n (%)	12 (57)
Race or ethnic group, n (%)	
White	10 (48)
Asian	7 (33)
Black or African-American	1 (5)
Not reported	3 (14)
ECOG PS, n (%)	
0	14 (67)
1	7 (33)
Tumor stage at screening, n (%)	
Metastatic	16 (76)
Locoregional	5 (24)
Baseline renal function, n (%)	
Creatinine clearance < 30 mL/min	0
Creatinine clearance 30 to < 60 mL/min	10 (48)
Creatinine clearance ≥ 60 mL/min	11 (52)

Data snapshot date: July 24, 2026.

^aIncludes 13 participants from safety lead in and 8 from Phase 1 expansion.

ECOG PS, Eastern Cooperative Oncology Group performance status; UC, urothelial cancer.

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	Cohort 7 (N = 21) ^a
Baseline hepatic function, n (%)	
Bilirubin ≤ upper limit of normal	21 (100)
Bellmunt risk factor, n (%)	
0	12 (57)
1	7 (33)
2	2 (10)
Site of disease at baseline, n (%)	
Visceral	13 (62)
Lung/pleura	8 (38)
Liver	4 (19)
Other visceral	4 (19)
Non-visceral	8 (38)
Lymph node only, n (%)	6 (29)
Median time since initial UC diagnosis, months (range)	5.9 (0.3-143.1)

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Safety Summary

Participants, n (%)	Cohort 7 (n = 21)
Median treatment duration (range), months	
SG	8.0 (0-18)
EV	7.6 (0-16)
ZIM	9.7 (0-20)
Any TEAE/grade ≥ 3 TEAE	21 (100)/14 (67)
Any TRAE/grade ≥ 3 TRAE	21 (100)/11 (52)

Participants, n (%)	Cohort 7 (n = 21)
TRAEs leading to any drug discontinuation	7 (33)
Discontinuation of SG	4 (19)
Discontinuation of EV	6 (29)
Discontinuation of ZIM	1 (5)
TEAE leading to death	0
DLT^a	1/12 (8)

- 3 participants died of disease progression; there were no treatment-related deaths

Data snapshot date: July 24, 2026.

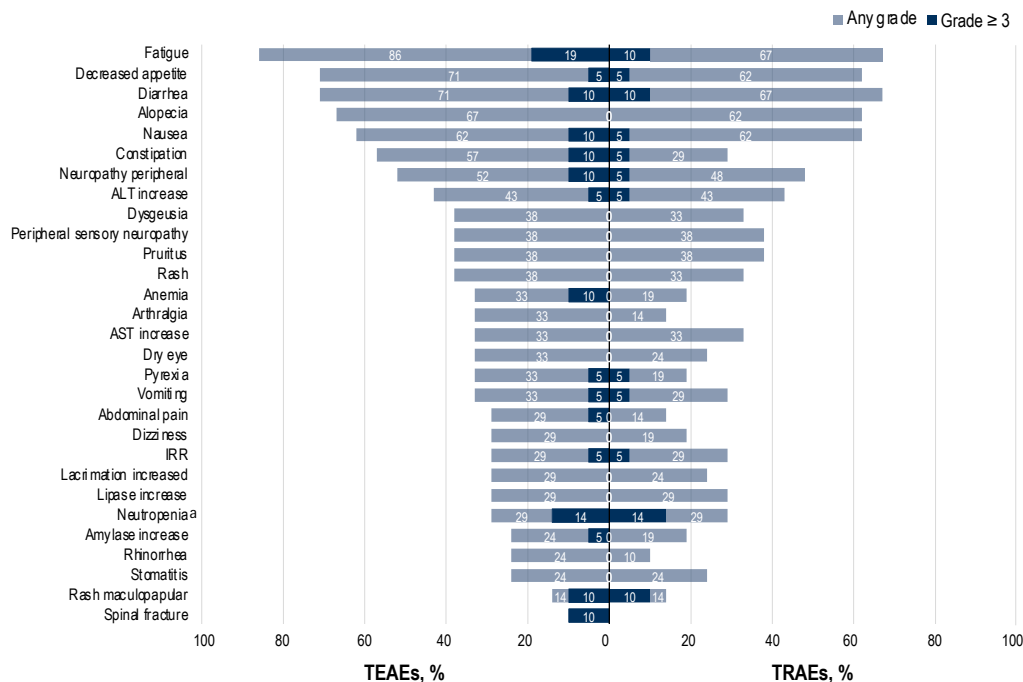
^a1/13 SLI participants was not DLT evaluable; the 1 DLT event was febrile neutropenia lasting < 24 hours.

AE, adverse event; DLT, dose-limiting toxicity; EV, enfortumab vedotin; SLI, safety lead-in; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; ZIM, zimberelimab.

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Most Common Treatment-Emergent vs Treatment-Related AEs



- The most common treatment-related AEs were fatigue, decreased appetite, diarrhea, alopecia, and nausea
- 20/21 (95%) participants received primary G-CSF prophylaxis from cycle 1. Grade 3 neutropenia^a was reported in 3/21 participants, including 1 participant who did not receive primary G-CSF prophylaxis. All three events occurred during cycle 1

Overall safety data were consistent with the known toxicity profile of SG, EV, and ZIM

Data snapshot date: July 24, 2026. TEAEs were included if they occurred in ≥ 20% (any-grade) or ≥ 10% (grade ≥ 3) of participants. ^aNeutropenia includes neutropenia, neutrophil count decreased, and febrile neutropenia.

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; EV, enfortumab vedotin; G-CSF, granulocyte colony-stimulating factor; IRR, infusion-related reaction; SLI, safety lead-in; SG, sacituzumab govitecan; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; ZIM, zimberelimab.

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Efficacy outcomes

Variable	Cohort 7 (n = 21)
Median follow-up (range), months	12.2 (1.3-20.8)
Objective response rate, ^a n (%) (95% CI)	17 (81) (58-95)
Best overall response, n (%)	
Complete response	3 (14)
Partial response	14 (67)
Stable disease	1 (5)
Stable disease ≥ 6 months	1 (5)
Progressive disease	1 (5)
Not evaluable/not assessed	2 (10)

Variable	Cohort 7 (n = 21)
Clinical benefit rate,^b n (%) (95% CI)	18 (86) (64-97)
Median DOR^c (95% CI), months	16.7 (4.9-NE)
9-month DOR, % (95% CI)	89 (43-98)
12-month DOR, % (95% CI)	76 (33-94)
Median time to response^d (range), months	2.5 (1.2-4.2)
Achieving response ≤3 months, n (%)	14/17 (82)
Median PFS (95% CI), months	19.3 (10.6-NE)
12-month PFS, % (95% CI)	73 (41-89)
Median OS (95% CI), months	NR (12.2-NE)

The combination of SG, EV, and ZIM demonstrated promising objective responses and survival outcomes

Data snapshot date: July 24, 2026.

Response rates and PFS were by investigator assessment. ^aObjective response rate is defined as the proportion of participants who achieved a best overall response of CR/PR. ^bClinical benefit rate is defined as proportion of participants with CR + PR + SD ≥ 6 months. ^cDuration of response is calculated based on the time between the first date showing a documented response of CR or PR and the date of progression or death. ^dTime to response is defined as time between the first dose date to the first documented PR/CR.

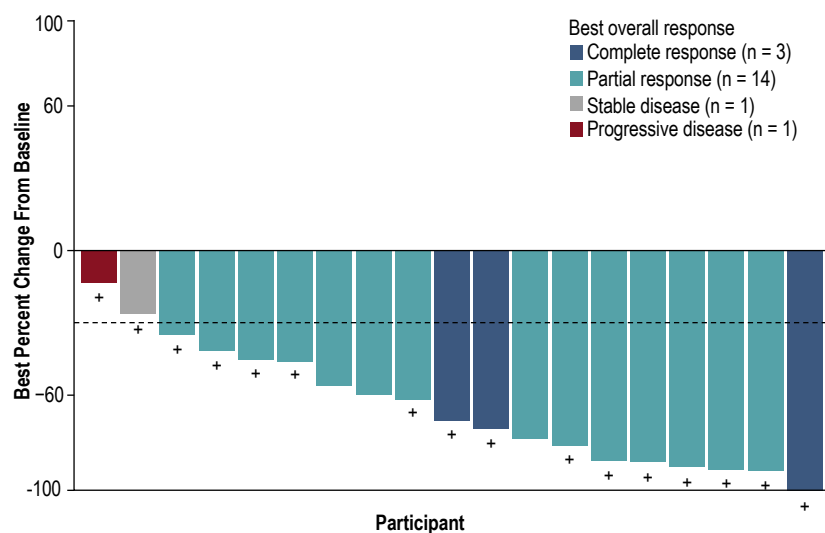
CR, complete response; DOR, duration of response; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; PR, partial response; SD, stable disease.

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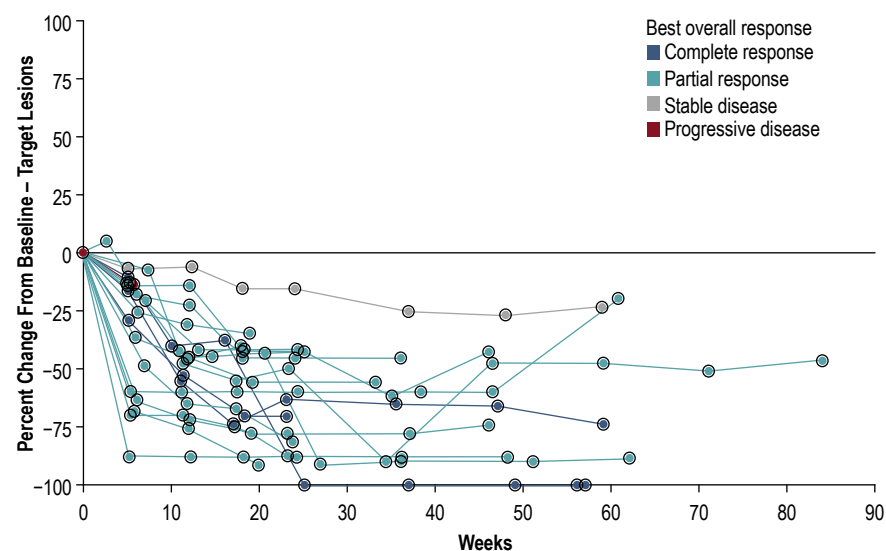
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Best Percent Change in Target Lesion Diameters and Tumor Response by Investigator Assessment

Best Percent Change from Baseline in Total Sum of Target Lesion Diameters



Spider Plot of Tumor Response per Investigator Assessment



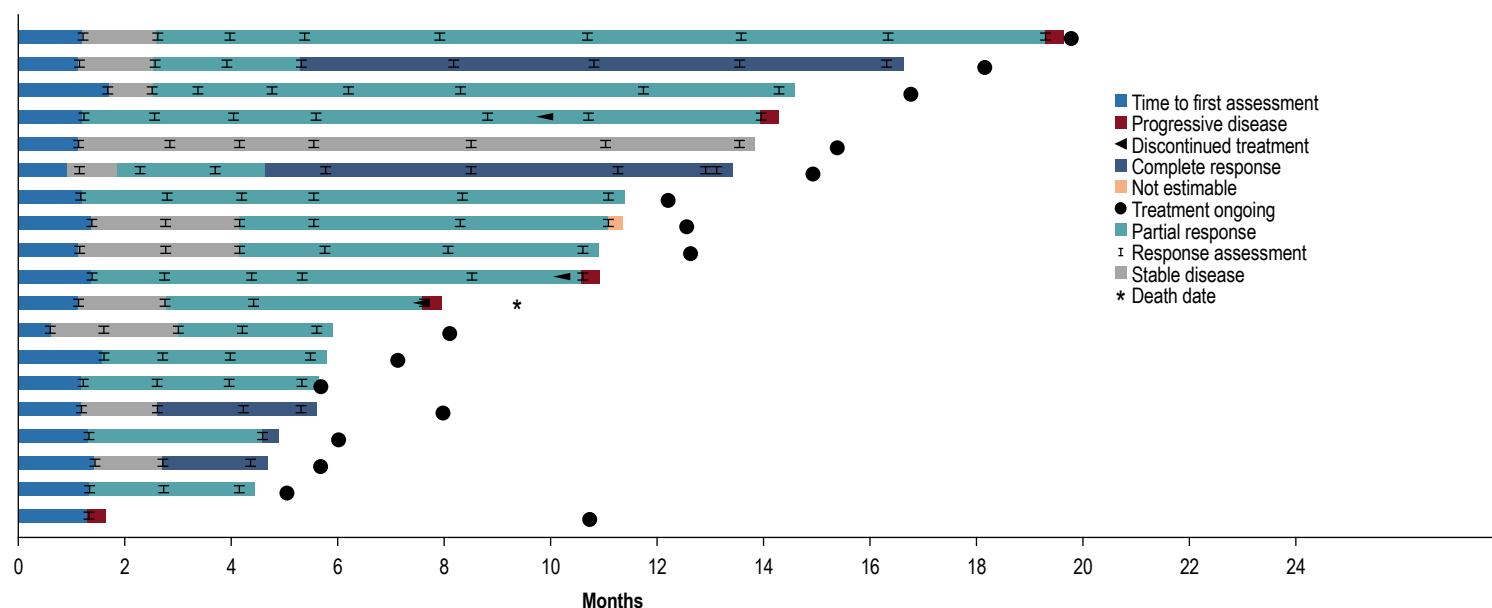
Tumor shrinkage occurred in all evaluable participants and the responses were durable

Data snapshot date: July 24, 2026.

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Swimmer Plot of Tumor Response by Investigator Assessment



Responses were sustained or deepened over time and most participants were still on treatment at the time of data snapshot

Data snapshot date: July 24, 2026.

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Conclusions

- SG + EV + ZIM showed manageable toxicity and tolerability over 12 months of median follow-up in participants with treatment-naïve mUC
 - No treatment-related deaths were observed
 - Discontinuation rate due to TRAEs for any agent was 33% (highest rate was reported for EV)
 - The overall safety findings were consistent with the established toxicity profiles of SG, EV, and ZIM
- SG + EV + ZIM demonstrated promising antitumor activity, with early and durable responses
 - Objective response was achieved in 81% of the participants; median DOR was 16.7 months
 - Median PFS was 19.3 months, and median OS was not reached
- These findings support further investigation of immunotherapy combinations that include ADCs with different mechanisms of action in patients with UC
 - Ongoing Gilead-supported studies of SG in combination with immunotherapy include the phase 2 DAD/DAD-IO (NCT04724018) study sponsored by the DFCI, and the phase 3 ECOG-ACRIN EA8231 (NCT06524544) study

DFCI, Dana-Farber Cancer Institute; EV, enfortumab vedotin; mUC, metastatic urothelial cancer; SG, sacituzumab govitecan; ZIM, zimberelimab.
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