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Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With SCLC

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in patients with small cell lung cancer (SCLC).

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Trodelvy is not indicated for use in patients with SCLC. The full indication, important safety information, and boxed warnings for neutropenia and diarrhea are available at: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

Summary

Clinical Studies in Patients With SCLC

TROPiCS-03 is a phase 2 study evaluating the efficacy and safety of SG in adult patients with metastatic solid tumors, including patients with histologically-confirmed ES-SCLC who progressed after no more than 1 prior line of PLT-based chemotherapy and anti–PD-(L)1 therapy. Results from the ES-SCLC cohort (n=43), with a median follow-up of 12.3 months showed that:[1]

- Investigator-assessed ORR (95% CI) was 41.9% (27–57.9), with 18 confirmed PRs.
- Investigator-assessed median DOR (95% CI) was 4.73 months (3.52–6.7) and 6-month DOR rate (95% CI) was 48.15% (23.86–68.88).
- Investigator-assessed median (95% CI) PFS and OS were 4.4 months (3.81–6.11), and 13.6 months (6.57–14.78), respectively.
- Investigator-assessed (95% CI) DCR and CBR were 83.7% (69.3–93.2), and 48.8% (33.3–64.5), respectively.
- The most frequent any-grade TEAEs were diarrhea (76.7%), fatigue (60.5%), neutropenia (55.8%), constipation (41.9%), nausea (39.5%), anemia (30.2%), and alopecia (30.2%). Grade ≥3 TEAEs were reported in 74.4% of patients; most frequent were neutropenia (44.2%), diarrhea (9.3%), hyponatremia (7%), anemia (4.7%), stomatitis (4.7%), and fatigue (2.3%).
- Based on the results from this study, the U.S. Food and Drug Administration (FDA) granted breakthrough therapy designation (BTD) for SG in adult patients with ES-SCLC whose disease progressed on or after platinum based chemotherapy.[2]

IMMU-132-01, a phase 1/2, single-arm, basket study investigated the efficacy and safety of SG in patients with metastatic epithelial cancers who had progressed on ≥1 prior therapy for metastatic disease. Patients received a median of 10 doses of SG, over a median (range) treatment duration of 2.5 (1–23) months. For the subset of patients with mSCLC:[3,4]

- ORR was 14% in the mSCLC ITT population (n=50) and 17% in the group that received SG 10 mg/kg (n=36).[4]

- The most common all-grade AEs in the mSCLC cohort (n=53) were diarrhea (53%), nausea (51%), fatigue (47%), neutropenia (43%), vomiting (34%), and abdominal pain (30%). The most common Grade ≥3 AEs were neutropenia (34%) and fatigue (13%).[4]
- Final efficacy results included an additional 12 patients not previously reported (n=62). ORR was 17%, median PFS was 3.7 months, and median OS was 7.1 months. To date, safety data specific to this cohort have not been published.[3]

Clinical Studies in Patients with SCLC

TROPiCS-03 Study in Metastatic Solid Tumors

Study design and demographics[1]

TROPiCS-03 is a multicohort, open-label, single-arm, phase 2 basket study evaluating the efficacy and safety of SG in adult patients with histologically confirmed metastatic or locally advanced solid tumors, including patients with ES-SCLC, who progressed after no more than 1 prior line of PLT-based chemotherapy and anti–PD-(L)1 therapy. Patients received SG 10 mg/kg IV on Days 1 and 8 of a 21-day treatment cycle, continued until progressive disease, unacceptable toxicity, withdrawal or death.

The primary endpoint was investigator-assessed ORR (confirmed CR or PR) per RECIST version 1.1. Key secondary endpoints included BICR-assessed ORR, DOR, CBR (confirmed CR + PR + SD ≥6 months), PFS, and investigator-assessed DOR, CBR and PFS. OS, safety, and DCR (CR + PR + SD) were also evaluated. In addition, efficacy was evaluated in the subgroups of patients with platinum resistant (CTFI <90 days) and platinum-sensitive (CTFI ≥90 days) disease.

Patients received a median (range) of 7 (1–25) treatment cycles. Median (range) duration of exposure to SG was 4.4 (0.03–18.04) months. Median (range) duration of follow-up was 12.3 (8.1–20.1) months. Seven patients (16.3%) were still receiving treatment, and 36 patients (83.7%) discontinued SG; the most common reason for discontinuation was PD in 31 patients (72.1%). The demographics and baseline characteristics are shown in Table 1.

Table 1. TROPiCS-03 (ES-SCLC Cohort): Demographics and Baseline Characteristics[1]

Variable		ES-SCLC Cohort (N=43)
Age, median (range), years		67 (48–83)
≥65 years, n (%)		26 (60.5)
Male, n (%)		20 (46.5)
Race or ethnic group, n (%)	White	36 (83.7)
	Black	2 (4.7)
	Asian	2 (4.7)
	Other/not specified/not reported[a]	3 (7)
Current or former tobacco use, n (%)		42 (97.7)
ECOG PS 0/1, n (%)		8 (18.6)/35 (81.4)
Metastatic disease stage IV at initial diagnosis, n (%)		40 (93)
Best response to most recent prior anticancer therapy, n (%)	CR/PR	24 (55.8)
	SD/PD	16 (37.2)
	Not available/not reported	3 (7)
Type of previous anticancer therapy[b], n (%)	Cisplatin and etoposide	7 (16.3)
	Carboplatin and etoposide	37 (86)
	Atezolizumab	32 (74.4)
	Durvalumab	10 (23.3)

Variable		ES-SCLC Cohort (N=43)
	Nivolumab	1 (2.3)
Chemotherapy-free interval, n (%)	<90 days (platinum-resistant)	20 (46.5)
	≥90 days (platinum-sensitive)	23 (53.5)
Metastatic disease sites, n (%)	Liver	13 (30.2)
	Brain	5 (11.6)

Abbreviation: ECOG PS=Eastern Cooperative Oncology Group performance status
[a]Other includes American Indian or Alaska Native; Native Hawaiian or other Pacific Islander; or other.
[b]One patient took cisplatin first and then switched to carboplatin because of toxicity.

Efficacy

Investigator-assessed efficacy outcomes, including outcomes by platinum-resistant and platinum-sensitive disease subgroups, are shown in Table 2.[1] BICR-assessed efficacy outcomes, including by platinum-resistant and platinum-sensitive disease subgroups, are shown in Table 3.[5] Investigator-assessed efficacy outcomes by age and sex are shown in Table 4.[5]

In those with post-baseline tumor assessment available, 33 patients (76.7%) had tumor shrinkage, and 21 patients (48.8%) had a reduction of >30%. Tumor shrinkage was observed in 21 patients with platinum-sensitive disease (CTFI ≥90 days), and in 12 patients with platinum-resistant disease (CTFI <90 days).[1]

Table 2. TROPiCS-03 (ES-SCLC Cohort): Efficacy by Investigator Assessment[1]

Outcomes		ES-SCLC Cohort (N=43)	CTFI <90 days (n=20)	CTFI ≥90 days (n=23)
ORR,[a] % (95% CI)		41.9 (27–57.9)	35 (15.4–59.2)	47.8 (26.8–69.4)
BOR, n (%)	Confirmed PR	18 (41.9)	7 (35)	11 (47.8)
	SD	18 (41.9)	7 (35)	11 (47.8)
	PD	4 (9.3)	4 (20)	0
	Not assessed	3 (7)	2 (10)	1 (4.3)
DCR,[b] % (95% CI)		83.7 (69.3–93.2)	70 (45.7–88.1)	95.7 (78.1–99.9)
CBR,[c] % (95% CI)		48.8 (33.3–64.5)	40 (19.1–63.9)	56.5 (34.5–76.8)
DOR,[d,e] median (95% CI), mo		4.73 (3.52–6.7)	6.31 (1.54–6.87)	4.44 (3.02–NR)
DOR rate at 6 mo,[d] % (95% CI)		48.15 (23.86–68.88)	57.14 (17.19–83.71)	41.56 (13.11–68.42)
PFS,[d] median (95% CI), mo		4.4 (3.81–6.11)	3.81 (1.38–7.56)	4.98 (4.07–7.43)
OS,[d] median (95% CI), mo		13.6 (6.57–14.78)	6.57 (4.73–17.71)	14.72 (7.72–NR)

[a]Patients with confirmed CR or PR per RECIST v1.1.
[b]Patients with confirmed PR + SD.
[c]Patients with confirmed PR + SD duration ≥6 months. SD duration was defined as the time from the date of the first dose of the study drug to the first documented PD or death from any cause.
[d]Based on Kaplan-Meier estimates.
[e]Calculated for patients with confirmed PR.

Table 3. TROPiCS-03 (ES-SCLC Cohort): Efficacy by BICR[5]

Outcomes per RECIST version 1.1		ES-SCLC Cohort (N=43)	CTFI <90 days (n=20)	CTFI ≥90 days (n=23)
ORR, % (95% CI)		44.2 (29.1–60.1)	35 (15.4–59.2)	52.2 (30.6–73.2)
BOR, n (%)	Confirmed CR	2 (4.7)	0	2 (8.7)
	Confirmed PR	17 (39.5)	7 (35)	10 (43.5)
	SD	19 (44.2)	9 (45)	10 (43.5)
	PD	2 (4.7)	2 (10)	0
	Not evaluable[a]	3 (7)	2 (10)	1 (4.3)
DCR.[b] % (95% CI)		88.4 (74.9–96.1)	80 (56.3–94.3)	95.7 (78.1–99.9)
CBR,[c] % (95% CI)		46.5 (31.2–62.3)	40 (19.1–63.9)	52.2 (30.6–73.2)
DOR,[d,e] median (95% CI), mo		5.39 (2.92–12.02)	4.67 (2.79–NR)	5.7 (2.79–NR)
PFS,[d] median (95% CI), mo		4.4 (3.19–6.67)	4.27 (2.66–5.55)	5.36 (3.06–7.46)

[a]Patients without any post-baseline assessment in the central imaging database.
[b]Patients with confirmed CR + PR + SD.
[c]Patients with confirmed CR + PR + SD duration ≥6 months. SD duration was defined as the time from the date of the first dose of study drug to first documented PD or death from any cause.
[d]Based on Kaplan-Meier estimates.
[e]For patients with confirmed CR and PR

Table 4. TROPiCS-03 (ES-SCLC Cohort): Investigator-Assessed Efficacy by Age and Sex[5]

Outcomes	Age		Sex	
	<65 years (n=17)	≥65 years (n=26)	Male (n=20)	Female (n=23)
ORR, % (95% CI)	35.3 (14.2–61.7)	46.2 (26.6–66.6)	60 (36.1–80.9)	26.1 (10.2–48.4)
PFS,[a] median (95% CI), mo	4.19 (2.63–6.11)	5.13 (3.81–7.56)	4.4 (2.79–7.62)	4.67 (2.66–6.11)
OS,[a] median (95% CI), mo	10.41 (4.73–17.71)	14.72 (6.57–NR)	14.72 (6.05–NR)	10.41 (5.68–14.78)

[a]Based on Kaplan-Meier estimates.

Safety[1]

TEAEs are shown in Table 5. No TEAEs led to discontinuation of SG. Grade ≥3 TEAEs occurred in 32 (74.4%) patients, and these were considered treatment-related in 26 patients (60.5%). Serious TEAEs occurred in 22 patients (51.2%), with febrile neutropenia being the most common (7%). TEAEs that led to dose reduction occurred in 16 patients (37.2%); the most frequent reasons for dose reduction were neutropenia (16.3%) and diarrhea (7%). TEAEs that led to treatment interruption occurred in 30 patients (69.8%). TEAEs led to death of 3 (7%) patients, with one death (neutropenic sepsis) deemed related to study drug.

Table 5. TROPiCS-03 (ES-SCLC Cohort): TEAEs Reported in ≥15% of Patients (N=43)[1]

TEAE, n (%)	Any-grade	Grade ≥3
Diarrhea	33 (76.7)	4 (9.3)
Fatigue	26 (60.5)	1 (2.3)
Neutropenia	24 (55.8)	19 (44.2)
Constipation	18 (41.9)	0
Nausea	17 (39.5)	0
Alopecia	13 (30.2)	0
Anemia	13 (30.2)	2 (4.7)
Decreased appetite	10 (23.3)	0
Abdominal pain	8 (18.6)	0
Hypomagnesemia	7 (16.3)	0

TEAE, n (%)	Any-grade	Grade ≥3
Rash	7 (16.3)	0
Vomiting	7 (16.3)	0

IMMU-132-01 Study in Metastatic Epithelial Cancer

Study design and demographics

IMMU-132-01, a phase 1/2, single-arm, multicenter, open-label basket study in adult patients (N=495) with metastatic epithelial cancer, included patients with mSCLC who had progressed after ≥1 previous treatment for metastatic disease.[3,4]

In an initial analysis of the mSCLC cohort, patients received SG 10 mg/kg (n=38) or 8 mg/kg (n=15) IV on Days 1 and 8 of a 21-day treatment cycle, continued until disease progression or unacceptable toxicity. Patients received a median of 10 doses of SG, over a median (range) treatment duration of 2.5 (1–23) months. Fifty-six percent of patients were female, and median (range) age was 63 (44–82) years. Patients received a median (range) of 2 (1–7) prior lines of therapy; all patients had received prior platinum and etoposide, 18 (34%) received prior topotecan and/or irinotecan, 9 (17%) received prior taxanes, and 5 (9%) received prior CPIs.[4]

Efficacy[4]

The ITT population (patients who had ≥2 doses and had their initial 8-week CT assessment) included 50 patients and the response-assessable population (≥2 doses and ≥1 post baseline CT response assessment) included 43 patients.

ORR according to RECIST version 1.1 (primary endpoint) in the mSCLC ITT cohort was 14% (7/50) and 17% (6/36) in the group that received SG 10 mg/kg. Median time (range) to response was 2 months (1.8–3.6). Additional efficacy outcomes are presented in Table 6.

Table 6. IMMU-132-01 (mSCLC Cohort): Efficacy Outcomes (ITT Population)[4]

Patient Responses		All Patients (N=50)	10 mg/kg (n=36)	8 mg/kg (n=14)
BOR, n (%)	PR	7 (14)	6 (17)	1 (7)
	SD	21 (42)	17 (47)	4 (29)
	PD	15 (30)	7 (19)	8 (57)
	Not evaluable	7 (14)	6 (17)	1 (7)
DOR, median (95% CI), mo		5.7 (3.6–19.9)	4 (3.6–5.7)	19.9[a]
CBR (PR+SD ≥4 mo), n (%)		17 (34)	14 (39)	3 (21)
PFS, median (95% CI), mo		3.7 (2.1–4.3)	3.7 (2.8–5.3)	2 (1.7–3.8)
OS, median (95% CI), mo		7.5 (6.2–8.8)	6.2 (5–8.3)	8.1 (7–22.4)

[a]n=1.

Of the 4 patients who received prior CPIs and had CT-assessable responses, 1 patient progressed, and 3 patients had SD.

Safety[4]

All-grade AEs (reported in >15% of patients) and Grade ≥3 AEs (reported in ≥2% of patients) are presented in Table 7. Grade ≥3 neutropenia which led to dose reductions occurred in 34% patients (15 patients in the 10 mg/kg group and 3 in the 8 mg/kg group). Ten patients received cytokine support for Grade ≥3 neutropenia (5 patients required cytokine support several times, and 5 patients required support one time only).

Table 7. IMMU-132-01 (mSCLC Cohort): All-Grade AEs (>20%) and Grade 3–4 AEs (>5%)[4]

AE, n (%)	All-Grade	Grade 3–4
Diarrhea	28 (53)	5 (9)
Nausea	27 (51)	–
Fatigue	25 (47)	7 (13)
Neutropenia	23 (43)	18 (34)
Vomiting	18 (34)	–
Abdominal pain	16 (30)	–
Anorexia	15 (28)	–
Anemia	14 (26)	3 (6)
Alopecia	12 (23)	–
Constipation	11 (21)	–

Final efficacy results: IMMU-132-01 (mSCLC cohort)[3]

Final efficacy results for ORR and additional efficacy outcomes from IMMU-132-01 included 12 patients not previously reported in the mSCLC cohort and are shown in Table 8. To date, safety data specific to this cohort have not been published.

Table 8. IMMU-132-01 (mSCLC Cohort): Response Rates[3]

Response Rates (n=62)							
ORR,% (95% CI)	CR, n (%)	PR, n (%)	SD, n (%)	DOR, median (95% CI), mo	OS, median (95% CI), mo	PFS, median (95% CI), mo	CBR, n (%) [95% CI]
17.7 (9.2–29.5)	0	11 (17.7)	24 (38.7)	5.7 (3.6–19.9)	7.1 (5.6–8.1)	3.7 (2.1–4.8)	15 (24.2) [14.2–36.7]

Ongoing Clinical Studies

EVOKE-SCLC-04

A global, multicenter, randomized, open-label, phase 3 study (NCT06801834) evaluating the efficacy and safety of SG versus topotecan in patients with previously treated ES-SCLC.

NCT06667167

A prospective, open-label, single-arm, phase 2 study (NCT06667167) in patients with ES-SCLC who were previously untreated for extensive disease. Patients will receive induction treatment with carboplatin, etoposide, and pembrolizumab, followed by maintenance treatment with SG and pembrolizumab.

References

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4. Gray JE, Heist RS, Starodub AN, et al. Therapy of small cell lung cancer (SCLC) with a topoisomerase-I-inhibiting antibody-drug conjugate (ADC) targeting Trop-2, sacituzumab govitecan. *Clin Cancer Res.* 2017;23(19):5711-5719.
5. Dowlati A, Chiang AC, Cervantes A, et al. Phase 2 open-label study of sacituzumab govitecan as second-line therapy in patients with extensive-stage SCLC: results from TROPiCS-03 [Supplementary Information]. *J Thorac Oncol.* 2025 Jan 2: S1556-0864(24)02549-8. doi: 10.1016/j.jtho.2024.12.028. Epub ahead of print.

Abbreviations

AE=adverse events
BICR= blinded independent central review
BOR=best overall response
CBR=clinical benefit rate
CPI=checkpoint inhibitor
CR=complete response
CTFI=chemotherapy-free interval
DCR=disease control rate
DOR=duration of response
ES-SCLC=extensive stage small cell lung cancer
mSCLC=metastatic small cell lung cancer
ORR=objective response rate
OS=overall survival
PD=progressive disease
PD-(L)1=programmed cell death-(ligand) 1
PFS=progression-free survival
PLT=platinum
PR=partial response
NR=not reached
RECIST=Response Evaluation Criteria in Solid Tumors
SCLC=small cell lung cancer
SD=stable disease
SG=sacituzumab govitecan
TEAE=treatment-emergent adverse event

Product Label

For the full indication, important safety information, and Boxed Warning(s), please refer to the Trodelvy US Prescribing Information available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.pdf.

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For any additional questions, please contact Trodelvy Medical Information at:

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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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