GILEAD | Medical Information

Trodelvy® (sacituzumab govitecan-hziy) First-Line Use in Cisplatin- or Platinum-Ineligible mUC

This document is in response to your request for information regarding the use of Trodelvy® (sacituzumab govitecan-hziy [SG]) in the first-line (1L) setting in patients with locally advanced or metastatic urothelial cancer (mUC) who are ineligible for cisplatin (cis)- or platinum-based therapy.

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Trodelvy is not indicated for use in patients with mUC. 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

Combination Therapy With SG in 1L Treatment of Cis-Ineligible mUC

A phase 1/2 non-randomized study evaluated the efficacy and safety of SG in combination with ipilimumab (IPI) + nivolumab (NIVO) in patients with treatment-naive, locally advanced or mUC who are ineligible to receive cis-based chemotherapy.[1,2]

- The recommended phase 2 dose (RP2D) from phase 1 was IPI 3 mg/kg + NIVO 1 mg/kg every 3 weeks for 4 cycles, followed by NIVO 3 mg/kg every 3 weeks + SG 8 mg/kg on Days 1 and 8 every 3 weeks.[2]
- In phase 2, the median (95% CI) progression-free survival (PFS) was 12.72 (9.17–not assessable [NA]) months, the duration of best response was 8.04 months, and the median (95% CI) overall survival (OS) was NA (11.05 months–NA) among the 18 patients with evaluable efficacy data at a median follow-up of 21.57 months.[2]
- The trial was terminated early due to 2 events of Grade 5 immune-mediated myocarditis. The most common any-grade treatment-related adverse events (TRAEs) were diarrhea (72%), rash (56%), fatigue (56%), nausea (52%), and neutropenia (52%).[2]

Combination Therapy With SG in 1L Treatment of Cis-Ineligible mUC

IPI + NIVO With SG as 1L Treatment for Cis-Ineligible mUC

Study design and demographics

A phase 1/2, non-randomized study evaluated the efficacy and safety of SG in combination with IPI + NIVO in patients with treatment-naive, locally advanced or mUC who are ineligible to receive cis-based chemotherapy.[1]

Phase 1 (N=9) evaluated the feasibility and tolerability of escalating doses of IPI + NIVO + SG to determine the maximum tolerated dose and the RP2D of the combination. In phase 1, patients were given fixed doses of IPI 3 mg/kg + NIVO 1 mg/kg every 3 weeks for 4 cycles, followed by NIVO 360 mg IV every 3 weeks. Beginning at Cycle 1, IV SG 8 mg/kg (Dose Level 1) was administered on Days 1 and 8 every 3 weeks with an allowance of 1 dose escalation to 10 mg/kg (Dose Level 2) and 1 dose reduction to 6 mg/kg. Three patients experienced dose-limiting toxicities: 2 who received SG 10 mg/kg (Grade 3 pneumonitis and Grade 3 skin rash) and 1 who received SG 8 mg/kg (Grade 3 skin rash).[1]

In phase 2, 16 patients received the RP2D of IPI 3 mg/kg + NIVO 1 mg/kg every 3 weeks for 4 cycles, followed by NIVO 3 mg/kg every 3 weeks + SG 8 mg/kg on Days 1 and 8 every 3 weeks. The objectives were objective response rate (ORR), PFS, OS, and duration of response.[2] Baseline demographics and disease characteristics of the patients in phase 1/2 are summarized in Table 1.

Table 1. Phase 1/2 Study of IPI + NIVO Followed by NIVO + SG: Baseline Demographics and Disease Characteristics[2]

Key Demographics and Characteristics	IPI + NIVO Followed by NIVO + SG (N=25)
Age, mean ± SD, years	71±7
Male, n (%)	19 (76)
Race, White/Black or African American, n (%)	9 (96)/1 (4)
ECOG PS, 0/1, n (%)	15 (65)/10 (35)
Site of metastases, visceral/lymph nodes/liver only, n (%)	16 (64)/8 (32)/1 (4)

Abbreviation: ECOG PS=Eastern Cooperative Oncology Group Performance Status.

Results[2]

With a median follow-up of 21.57 months, the ORR in the efficacy analysis set (n=18) was 83.3%. Six patients had a complete response, 9 patients had a partial response, 1 patient had progressive disease (ie, emergence of a new lesion with a reduction of the target lesion), and 2 patients had stable disease. The median (95% CI) PFS was 12.72 (9.17–NA) months, and the median (95% CI) OS was NA (1.05 months–NA). The duration of best response was 8.04 months.

The trial was terminated early due to 2 events of Grade 5 immune-mediated myocarditis. The most common (>20%) any-grade and Grade ≥3 TRAEs are presented in Table 2.

Table 2. Phase 1/2 Study of IPI + NIVO Followed by NIVO + SG: Most Common (>20%) TRAEs[2]

TRAE, n (%)	Any-Grade	Grade ≥3
Diarrhea	18 (72)	3 (12)
Rash	14 (56)	6 (24)
Fatigue	14 (56)	1 (4)
Neutropenia	13 (52)	7 (28)
Nausea	13 (52)	0
Hypokalemia	11 (44)	4 (16)
Hypophosphatemia	10 (40)	0
Anemia	7 (28)	5 (20)
Vomiting	6 (24)	2 (8)
Abdominal pain	6 (24)	1 (4)
Pruritus	6 (24)	1 (4)
Constipation	6 (24)	0
Edema	6 (24)	0

References

1. Jain RK, Yang Y, Chadha J, et al. Phase I/II study of Ipilimumab plus Nivolumab (IPI-NIVO) combined with sacituzumab govitecan in patients with metastatic cisplatin-ineligible urothelial carcinoma [Poster 521]. Paper presented at: American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium; 16-18 February, 2023; San Francisco, CA.
2. Jain RK, Ong F, Chatwal M, et al. Phase 1/2 study of ipilimumab plus nivolumab (IPI-NIVO) combined with sacituzumab govitecan in patients with metastatic cisplatin-ineligible urothelial carcinoma [Poster 1969P]. Paper presented at: European Society for Medical Oncology (ESMO); September 13-17, 2024; Barcelona, Spain.

Product Label

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

Follow-Up

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

☎1-888-983-4668 or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or 🖱 www.gilead.com/utility/contact/report-an-adverse-event

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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