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Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With mCRPC Progressing on ARSIs

This document is in response to your request for information regarding Trodelvy® (sacituzumab govitecan-hziy [SG]) and its use in patients with metastatic castration-resistant prostate cancer (mCRPC) progressing on androgen receptor signaling inhibitors (ARSIs).

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Trodelvy is not indicated for use in patients with mCRPC. 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.

Clinical Study in Patients With mCRPC Progressing on ARSIs

Study Design and Demographics

An ongoing, open-label, phase 2 study (NCT03725761) is evaluating the use of SG in patients with mCRPC progressing on ARSIs. Eligibility criteria included patients with mCRPC who had increasing prostate-specific antigen (PSA) levels and radiographic progression during treatment with abiraterone acetate or enzalutamide. After a 4-week washout period, SG 10 mg/kg was administered on Days 1 and 8 of a 21-day treatment cycle until radiographic disease progression, initiation of alternative therapy, unacceptable toxicity, or withdrawal of consent. SG was given in addition to their previous ARSI.[1,2]

The two primary endpoints evaluated were radiographic progression-free survival (rPFS) at Month 6 and decrease in PSA level of ≥50% (PSA50 response).[1] Secondary outcome measures will include the median PFS (at 6 months and up to 2 years), radiologic response rate (decrease in tumor size relative to baseline), median overall survival, and safety.[2]

For patients who did not have disease progression, PSA level monitoring and bone scans and/or CT scans were performed every 3 months (or according to standard of care) for up to 2 years or until disease progression or initiation of other treatment. Liquid biopsies were collected at baseline, at Cycle 1, Day 8, and with every third cycle until disease progression occurred.[1]

Thirty-one patients were included in the final clinical analysis; patients had a median PSA of 30 ng/mL at baseline.[1] Additional demographics and characteristics are shown in Table 1.

Table 1. Baseline Demographics and Disease Characteristics (Lang et al)[1]

Key Demographics and Characteristics		Overall (N=31)	Chemotherapy Naïve (n=25)	Chemotherapy Exposed (n=6)
Age, median (range), years		68 (54–82)	68 (56–82)	62 (54–72)
Race, n (%)	White	25 (81)	21 (84)	4 (67)
	Black or African American	2 (6)	2 (8)	0
	Asian	2 (6)	1 (4)	1 (17)
	Unknown	2 (6)	1 (4)	1 (17)
PSA level, median (range), ng/mL		30 (3–3852)	30 (3–3852)	46 (4–96)

Final Clinical Results

Efficacy[1]

The overall 6-month rPFS rate was 52%, with a median (95% CI) rPFS of 6.1 (3.1–10.1) months. The corresponding 6-month rPFS rate among patients who were naïve to chemotherapy was 68%, with a median (95% CI) rPFS of 8.3 (5.7–not reached) months. The longest duration of SG-only treatment was 14 months.

None of the patients who were receiving SG monotherapy had PSA50 responses; however, stable PSA levels were associated with the achievement of 6-month rPFS in these patients. Two of the 3 patients who received SG + ARSIs had PSA50 responses: each had hyperactive AR signaling and bone-only metastases, and were chemotherapy-naïve; 1 patient stopped treatment due to fatigue, and the other was continuing treatment (beyond Cycle 11).

Safety

The most common (n>5) Grade 3/4 AEs reported were neutrophil count decreased, anemia, and diarrhea (Table 2). Three episodes of Grade 3 febrile neutropenia occurred.[1]

Table 2. Final Clinical Results (N=31): Grade 3/4 AEs (Lang et al)[1]

AEs, n	Grade 3	Grade 4
Neutrophil count decreased	12	9
Anemia	8	0
Diarrhea	6	0
WBC decreased	3	2
Febrile neutropenia	3	0
Alkaline phosphatase increased	1	0
Nausea	1	0
Syncope	1	0
Typhlitis	1	0
Vasovagal reaction	1	0

Liquid biopsy results[1]

Patients who had a higher expression of genes related to androgen receptors (ARs) and neuroendocrine (NE) differentiation at baseline were not responders to SG (median PFS: 2.36 months). Patients with higher AR transcriptional activity were responders to SG (median PFS: 8.78 months), and those with low AR activity and mixed NE differentiation had a median PFS of 5.72 months.

Higher trophoblast antigen 2 (Trop-2) expression (>10 Trop-2 circulating tumor cells [CTCs]/7.5 mL) at baseline was associated with longer rPFS (≥6 months vs <6 months) compared with those who had lower Trop-2 expression. Among patients who had rPFS >6 months, circulating tumor DNA content and Trop-2 expression decreased numerically during treatment (Cycle 3, Day 1). Among these patients, samples collected at the end of treatment revealed no Trop-2 whereas the number of epithelial cell adhesion molecule CTCs increased, which was associated with AR transcriptional activity as well as NE prostate cancer markers. Further, the conversion from high AR signaling or AR-variant status at baseline to being AR-negative at Cycle 3, Day 1 was associated with rPFS >6 months.

References

1. Lang JM, Sperger J. M., Kyriakopolous CE, et al. Final clinical and liquid biopsy (LBx) results of phase 2 trial of sacituzumab govitecan (SG) in patients (Pts) with metastatic castration resistant prostate cancer (mCRPC) progressing on androgen receptor pathway inhibitors (ARPIs) [Poster 1648P]. Paper presented at: European Society for Medical Oncology (ESMO) Congress; 13-17 September 2024; Barcelona, Spain.
2. ClinicalTrials.gov. IMMU-132 in Patients With Metastatic Castration-Resistant Prostate Cancer Progressing on Second Generation AR-Directed Therapy. ClinicalTrials.gov Identifier: NCT03725761. Available at: https://clinicaltrials.gov/ct2/show/NCT03725761.

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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