Abstract 376

Clinical Benefit of Mirvetuximab Soravtansine in Ovarian Cancer Patients With High Folate Receptor Alpha Expression: Results From the SORAYA Study

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BACKGROUND AND OBJECTIVE

- Treatment options for platinum-resistant ovarian cancer (PROC) are limited, consisting primarily of single-agent chemotherapy, and the majority of patients will have received prior bevacizumab[1,2]
  - Single-agent chemotherapy has limited activity (ORR, 4%–13%) along with considerable toxicity[3-6]
- Folate receptor alpha (FRα), also known as folate receptor 1 (FOLR1), has limited expression on normal tissues but is elevated in most ovarian cancers, which makes FRα an attractive target for the development of novel therapies[7,8]
- Mirvetuximab soravtansine (MIRV) is an antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and a maytansinoid DM4 payload, a potent tubulin-targeting agent[9]
- SORAYA is a global, single-arm, phase 3 study that evaluated MIRV for the treatment of PROC in patients with FRα-high expression who received 1 to 3 prior therapies, including required prior bevacizumab[10-12]
- Treatment with MIRV demonstrated clinically meaningful antitumor activity regardless of the number of prior lines of therapy or prior PARPi use[10,11]
  - Previous data for ORR: 32.4% (34 of 105) of patients, including 5 CR[10]
  - Previous data for median DOR: 6.9 months (95% CI, 5.6–9.7)[10]
- Here we report updated data on the clinical benefit of MIRV, including tumor reduction and disease control rate (data cutoff = April 29, 2022)

Methods

- The efficacy-evaluable population consisted of 105 patients who had measurable disease at baseline by investigator assessment per Response Evaluation Criteria in Solid Tumors, version 1.1 (RECIST v1.1)
- The safety population contained 106 patients who received ≥1 dose of MIRV

Table 1. SORAYA Study Design

Enrollment and Key Eligibility Criteria

- Enrolled 106 patients
- At least 1 lesion that met RECIST v1.1 criteria for measurable disease
- Platinum-resistant disease (PFI ≤6 mo)
  - Primary platinum-refractory disease excluded (primary PFI <3 mo)
- Prior bevacizumab required; prior PARPi allowed
- 1–3 prior lines of therapy
- Patients with *BRCA* mutations allowed
- FRα high (≥75% of cells staining positive with ≥2+ staining intensity)[a]

MIRV Dosing

- Patients received MIRV 6 mg/kg, AIBW,[b] IV once every 3 weeks

Primary Endpoint

- Confirmed ORR by investigator assessment

Secondary Endpoints[c]

- DOR
- Safety and tolerability
- PFS
- OS
- ORR, DOR, and PFS by BICR as sensitivity analyses
- CA-125 response by GCIG criteria

Exploratory Endpoints

- DCR
- Tumor reduction

Statistical Assumptions

- The study was designed to test the null hypothesis that the ORR was 12%, based on ORR for single-agent chemotherapy in prior trials of PROC (range, 4%–13%)
- Ninety percent power to detect a difference in ORR of 12% (24% vs 12%) in sample size of 105 efficacy-evaluable patients using 1-sided binomial test and 1-sided α level of 0.025
- Enrollment was planned for approximately 110 patients, resulting in approximately 105 efficacy-evaluable patients

[a]PS2- scoring method, sum of staining of 2+ and 3+ intensity. [b]AIBW, also known as AdjBW, is calculated as IBW (kg) + 0.4 (actual weight – IBW). IBW for females is calculated as 0.9*height (cm)-92. [c]Secondary endpoints were evaluated to further characterize the efficacy of MIRV. No formal hypothesis testing was performed on secondary endpoints.

Patient Demographics and Characteristics

Table 2. Baseline Demographics and Clinical Characteristics

Characteristics		All patients (N=106)
Age, median (range)	Age in years	62 (35–85)
Primary cancer diagnosis, n (%)[a]	Epithelial ovarian cancer Fallopian tube cancer Primary peritoneal cancer	85 (80) 8 (8) 12 (11)
Stage at initial diagnosis, n (%)[b]	I–II III IV	2 (2) 63 (59) **40 (38)**
ECOG PS, n (%)	0 1	60 (57) 46 (43)
***BRCA* mutation, n (%)**	Yes No/unknown	21 (20) 85 (80)
No. of prior systemic therapies (%)	1 2 3[c]	10 (9) 41 (39) **55 (52)**
Prior exposure, n (%)	Bevacizumab PARPi Taxanes	**106 (100)** **51 (48)** 105 (99)
Primary platinum-free interval, n (%)	3–12 mo[d] >12 mo	63 (59) 43 (41)
Platinum-free interval, n (%)	0–3 mo 3– >6 mo	**39 (37)** 67 (63)

[a]Primary cancer diagnosis includes 1 patient with serous tubal intraepithelial carcinoma. [b]One patient missing information for stage at initial diagnosis; none of the patients were at stage II when initially diagnosed. [c]Includes 1 patient with >3 prior lines. [d]Includes 1 patient with primary platinum-free interval of 2.8 months.

Results: Response-Related Efficacy

Table 3. Investigator Assessment

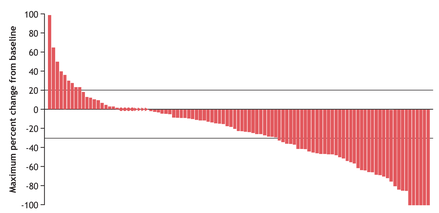
	Overall (N=105[a])	Exposure: Prior PARPi (n=50)	Exposure: PARPi naïve (n=51)	Exposure: 1–2 prior lines (n=51)	Exposure: 3 prior lines (n=53)
ORR, n (%) (95% CI)	34 (32.4) (23.6–42.2)	19 (38.0) (24.7–52.8)	14 (27.5) (15.9–41.7)	18 (35.3) (22.4–49.9)	16 (30.2) (18.3–44.3)
Best overall response, n (%)					
CR	5 (4.8)	2 (4.0)	2 (3.9)	2 (3.9)	3 (5.7)
PR	29 (27.6)	17 (34.0)	12 (23.5)	16 (31.4)	13 (24.5)
SD	48 (45.7)	17 (34.0)	30 (58.8)	24 (47.1)	24 (45.3)
PD	20 (19.0)	13 (26.0)	5 (9.8)	9 (17.6)	10 (18.9)
NE	3 (2.9)	1 (2.0)	2 (3.9)	0	3 (5.7)
Median DOR[b], mo (95% CI)	6.9 (5.6–9.7)	5.7[c] (3.5–9.6)	6.4[d] (3.0–NR)	5.9[e] (4.2–9.6)	7.4[f] (3.5–10.7)
DCR[g], n (%) (95% CI)	54 (51.4) (41.5–61.3)	27 (54.0) (39.3–68.2)	26 (51.0) (36.6–65.2)	30 (58.8) (44.2–72.4)	24 (45.3) (31.6–59.6)
Tumor reduction, n (%)	75 (71.4)	37 (74.0)	36 (70.6)	39 (76.5)	36 (67.9)

- 51% of patients had disease control (defined as CR, PR, or SD for ≥12 weeks)

[a]Efficacy-evaluable population. [b]Median DOR for overall patients was calculated among patients with CR (n=5) or PR (n=29) only. [c]n=19. [d]n=14. [e]n=18. [f]n=16. [g]Duration of SD is from the date of first dose to the date of last tumor assessment prior to PD or death. If the duration of SD was ≥12 weeks, the DCR analysis categorized the patient as having disease control.

Results: Tumor Reduction and Disease Control Rate

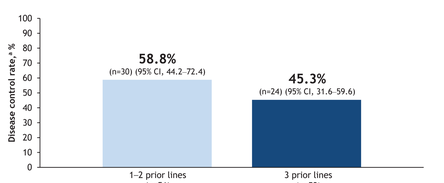
Figure 1. Best Tumor Response by RECIST (n=102[a])



[a]Three patients had no postbaseline tumor assessment.

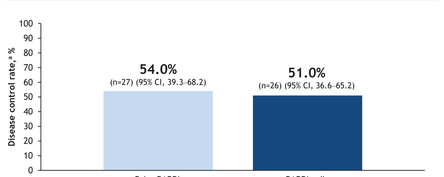
- 71% of patients experienced tumor reduction as their best response
- Tumor reduction occurred in 39 (76.5%) patients with 1 to 2 prior lines of and in 36 (67.9%) patients with 3 prior lines of therapy
- Tumor reduction occurred in 37 (74.0%) of patients with prior PARPi exposure and 36 (70.6%) of patients without prior PARPi exposure

Figure 2. Disease Control Rate by Number of Prior Therapies



[a]Duration of SD is from the date of first dose to the date of last tumor assessment prior to PD or death. If the duration of SD was ≥12 weeks, the DCR analysis categorized the patient as having disease control.

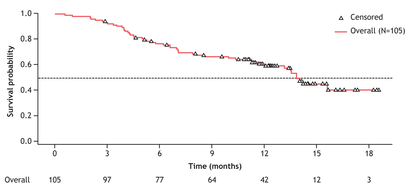
Figure 3. Disease Control Rate by Prior PARPi Status



[a]Duration of SD is from the date of first dose to the date of last tumor assessment prior to PD or death. If the duration of SD was ≥12 weeks, the DCR analysis categorized the patient as having disease control.

Results: Overall Survival

Figure 4. Kaplan-Meier Plot for Overall Survival[a] (Investigator Assessed)

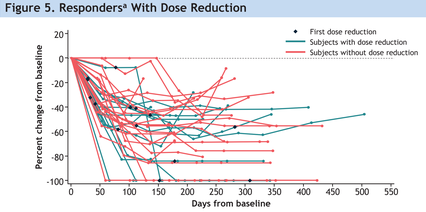


[a]Overall survival was defined as the time from the date of first dose until the date of death from any cause.

- Median OS was 13.8 months (95% CI, 12.0–not estimable) with 46% of events reported

Results: Responders With Dose Reduction

Figure 5. Responders[a] With Dose Reduction



[a]Responders included patients with CR (n=5) or PR (n=29) only.

- In responders, depth and duration of response did not appear to be affected by dose reductions
- At data cutoff, 5 responders were still receiving MIRV

Results: Treatment-Related Adverse Events

Table 4. Treatment-Related Adverse Events (≥10%) (N=106)

TRAEs, n (%)	All grades	Grade 3	Grade 4
Blurred vision	43 (41)	6 (6)	0
Keratopathy[a]	31 (29)	8 (8)	1 (1)
Nausea	31 (29)	0	0
Dry eye	26 (25)	2 (2)	0
Fatigue	25 (24)	1 (1)	0
Diarrhea	23 (22)	2 (2)	0
Asthenia	16 (15)	1 (1)	0
Photophobia	14 (13)	0	0
Peripheral neuropathy[b]	14 (13)	0	0
Decreased appetite	14 (13)	1 (1)	0
Neutropenia	14 (13)	2 (2)	0
Vomiting	12 (11)	0	0

[a]The grouped preferred term "Keratopathy" includes the following preferred terms: corneal cyst, corneal disorder, corneal epithelial microcysts, keratitis, keratopathy, limbal stem cell deficiency, corneal opacity, corneal erosion, corneal pigmentation, corneal deposits, keratitis interstitial, and punctate keratitis. [b]Peripheral neuropathy includes the following preferred terms: neuropathy peripheral, peripheral sensory neuropathy, peripheral motor neuropathy, paresthesia, and hypoesthesia.

Results: Treatment-Related Adverse Events (cont)

- Adverse events were primarily low-grade, reversible ocular and gastrointestinal events
- Serious (grade ≥3) treatment-related adverse events (TRAEs) occurred in 9% of patients
- TRAEs led to dose delay in 33% of patients and dose reduction in 20% of patients
- Ten patients (9%) discontinued treatment due to TRAEs
  - One patient discontinued due to an ocular TRAE
- One death was recorded as possibly related to study drug
  - Respiratory failure (autopsy found lung metastases and no evidence of drug reaction)

Results: Ocular Adverse Events

- In this dataset, 55 of 106 patients (52%) had any reported ocular event (blurred vision or keratopathy; all grades)
  - 43 patients (41%) experienced ocular events that were grade 2 or lower in severity; 12 patients (11%) experienced a grade ≥3 ocular event
- Onset of ocular events typically occurred during cycle 2 of treatment (median time to onset, 1.3 months)
  - Median time to onset of vision blurred was 1.3 months (range, 0.0-9.9), and median time to onset of keratopathy was 1.5 months (range, 1.1-8.6)
- At data cutoff, 96.2% of patients with grade ≥2 blurred vision or keratopathy events had resolution to grade 1 or 0
- One of 106 patients (<1%) discontinued MIRV due to an ocular event

CONCLUSIONS

- MIRV monotherapy for the treatment of PROC resulted in clinically meaningful antitumor activity including: disease control rate with durable response and preliminary overall survival, in heavily pretreated patients with FRα-high expression
  - 71% experienced tumor reduction
  - 51% had disease control (CR, PR, or SD for ≥12 weeks)
  - Median OS was 13.8 months
- Dose reductions did not impact the depth and duration of tumor reduction in responders
- Safety and tolerability of MIRV in SORAYA are consistent with that observed in previous studies[13]
  - Adverse events were primarily low-grade gastrointestinal and ocular events that generally resolved with supportive care or, if needed, dose modifications
  - The discontinuation rate due to TRAEs was 9%
- In the SORAYA study, MIRV demonstrated a favorable benefit-risk profile in patients with FRα-high PROC

These results demonstrate that MIRV has the potential to be a practice-changing, biomarker-driven therapy

Abbreviations: ADC, antibody-drug conjugate; AdjBW, adjusted body weight; AIBW, adjusted ideal body weight; BICR, blinded independent central review; *BRCA*, BReast CAncer gene; CA-125, cancer antigen 125; CR, complete response; DCR, disease control rate; DM4, N2′-[4-[(3-carboxypropyl)dithio]-4-methyl-1-oxo-2-sulfopentyl]-N2′-deacetylmaytansine; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; *FOLR1*, folate receptor 1; FRα, folate receptor alpha; GCIG, Gynecologic Cancer Intergroup; IBW, ideal body weight; IV, intravenously; MIRV, mirvetuximab soravtansine; mo, months; NE, not evaluable; NR, not reached; ORR, objective response rate; OS, overall survival; PARPi, poly (ADP-ribose) polymerase inhibitor; PD, progressive disease; PFI, platinum-free interval; PFS, progression-free survival; PR, partial response; PROC, platinum-resistant ovarian cancer; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; SD, stable disease; TRAEs, treatment-related adverse events.

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