Abstract 499

Mirvetuximab Soravtansine and Carboplatin for Treatment of Patients With Recurrent Folate Receptor Alpha–Positive Platinum-Sensitive Ovarian Cancer: A Final Analysis

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BACKGROUND

- 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[1,2]
- Mirvetuximab soravtansine (MIRV) is a first-in-class antibody-drug conjugate (ADC) comprising an FRα-binding antibody, cleavable linker, and maytansinoid DM4 payload, a potent tubulin-targeting agent[3,4]
- MIRV has shown clinically meaningful antitumor activity in patients with platinum-resistant ovarian cancer as a single agent and in combination therapy[4–6]
- As part of the phase 1b/2 FORWARD II trial (NCT02606305), MIRV combined with carboplatin (carbo) was evaluated in patients with recurrent FRα-positive platinum-sensitive ovarian cancer[7,8]
- Here we report the final safety and efficacy analysis of this combination regimen

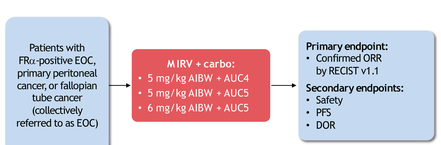
Objectives

- To analyze the safety and efficacy of MIRV combined with carbo in patients with FRα-positive platinum-sensitive ovarian cancer

Methods

- The phase 1b/2 study, FORWARD II, evaluated the safety, tolerability, and preliminary activity of MIRV combinations in patients with FRα-positive recurrent ovarian cancer[7]
  - MIRV + carbo was administered on day 1 of a 21-day cycle for 6 or more cycles per the investigator[8]
  - If the patient had at least stable disease per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1), then continue MIRV every 3 weeks until intolerable toxicity or AEs, disease progression, or investigator/patient decision[8]

Figure 1. Trial Schema



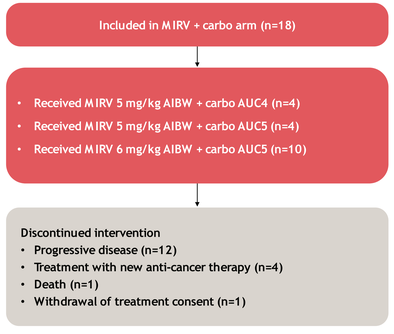
Methods (continued)

- This study enrolled adult patients with ≥1 lesion that meets the definition of measurable disease according to RECIST v1.1 and FRα-positive (defined by immunohistochemistry with ≥25% of tumor cells with ≥2+ staining intensity)
- Patients had disease that was platinum-sensitive (ie, responded to platinum therapy and did not progress within 6 months of completing treatment)
- Patients received MIRV combined with carbo intravenously on day 1 of a 3-week cycle using a standard 3 + 3 design, with a starting dose of MIRV 5 mg/kg AIBW and carbo AUC4[7]

Patient Disposition

- At data cutoff (June 21, 2021), 18 patients received MIRV + carbo

Figure 2. Patient Disposition in the MIRV + Carbo Arm



Median (range) duration of MIRV dosing

- MIRV 5 mg/kg AIBW + carbo AUC4: 59.5 wks (43.0–149.1)
- MIRV 5 mg/kg AIBW + carbo AUC5: 42.5 wks (9.0–238.3)
- MIRV 6 mg/kg AIBW + carbo AUC5: 62.3 wks (7.0–140.0)

Median (range) duration of carbo dosing

- MIRV 5 mg/kg AIBW + carbo AUC4: 31.0 wks (12.0–39.0)
- MIRV 5 mg/kg AIBW + carbo AUC5: 14.50 wks (9.0–22.0)
- MIRV 6 mg/kg AIBW + carbo AUC5: 27.0 wks (7.0–52.1)

Baseline Demographics and Characteristics

Table 1. Baseline Demographics and Disease Characteristics

	Patients (n=18)
Median age (range), y	66 (47–82)
Race and ethnicity, n (%)	
White	18 (100)
ECOG PS, n (%)	
0	7 (39)
1	11 (61)
Primary diagnosis, n (%)	
Epithelial ovarian cancer	16 (89)
Fallopian tube cancer	2 (11)
Stage at initial diagnosis, n (%)	
III	12 (67)
IV	6 (33)
FRα expression level per protocol, n (%)[a]	
Low	7 (39)
Medium	4 (22)
High	7 (39)
No. of prior therapies (%)	
1–2	11 (61)
3	4 (22)
4+	3 (17)
Prior therapy, n (%)	
Platinum	18 (100)
Taxanes	18 (100)
PARP inhibitor	7 (39)
Bevacizumab	5 (28)

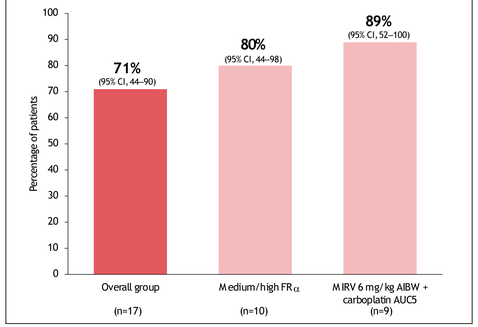
[a]PS2 scoring: high, ≥75% of tumor cells with ≥2+ staining intensity; medium, 50% to 74% of tumor cells with ≥2+ staining intensity; low, 25% to 49% with ≥2+ staining intensity.

Results: Efficacy

- The ORR in the overall efficacy evaluable patient group was 71% (12 of 17); 18% (n=3) of patients had a complete response, and 53% (n=9) had a partial response (Figure 3)
  - The ORR was 89% in patients receiving MIRV 6 mg/kg AIBW + carbo AUC5 (n=9), 44% (n=4) of whom were classified as FRα medium or high
  - The ORR was 80% in the medium/high-FRα subgroup (n=10) and 57% in the low-FRα subgroup (n=7)
- The median DOR was 12.1 months (95% CI, 5.7–27.5) in the responders (n=12)
  - The median DOR was 12.1 months (95% CI, 4.4–NE) in patients receiving MIRV 6 mg/kg AIBW + carbo AUC5 (n=8)
  - The median DOR was 24.2 months (95% CI, 6.1–54.3) and 8.9 months (95% CI, 4.4–NE) in the medium/high-FRα (n=8) and low-FRα (n=4) subgroups, respectively
- The median PFS estimate was 16.4 months (95% CI, 10.4–30.2) in the overall group (n=17)
  - The median PFS was 16.5 months (95% CI, 7.0–NE) in patients receiving MIRV 6 mg/kg AIBW + carbo AUC5 (n=9)
  - The median PFS was 15.0 months (95% CI, 10.4–55.5) in the medium/high-FRα subgroup (n=10) and 16.5 months (95% CI, 7.0–NE) in the low-FRα subgroup (n=7)

Results: Efficacy (continued)

Figure 3. ORR in the Overall Group, Medium/High-FRα Subgroup, and Patients Receiving MIRV 6 mg/kg AIBW + Carbo AUC5



Results: Safety and Tolerability

Table 2. Most Common TRAEs Reported in ≥20% of Patients (N=18)

	All grades	Grade 3	Grade 4
Nausea	13 (72)	0	0
Blurred vision	12 (67)	0	0
Thrombocytopenia	11 (61)	3 (17)	0
Diarrhea	10 (56)	1 (6)	0
Neutropenia	10 (56)	4 (22)	1 (6)
Fatigue	10 (56)	2 (11)	0
Vomiting	8 (44)	0	0
Hypokalemia	8 (44)	2 (11)	0
Hypomagnesemia	7 (39)	0	0
Anemia	6 (33)	1 (6)	0
Peripheral sensory neuropathy	6 (33)	0	0
Pneumonitis	6 (33)	1 (6)	0
Dry eye	5 (28)	0	0
Headache	5 (28)	0	0
Myalgia	5 (28)	0	0
ALT increased	5 (28)	0	0
AST increased	5 (28)	0	0
Decreased appetite	4 (22)	0	0
Cough	4 (22)	0	0

Data are n (%).

Results: Safety and Tolerability (continued)

- 72% (n=13) of patients continued with MIRV maintenance therapy
- The most common non-ocular treatment-related AEs (TRAEs; all grades) occurring in ≥50% of patients were nausea, thrombocytopenia, diarrhea, neutropenia, and fatigue
- Ocular TRAEs that occurred in ≥20% of patients were blurred vision and dry eye, all events grade 1 or 2
- Grade ≥3 TRAEs occurred in 56% of patients, the most common of which were neutropenia, thrombocytopenia, fatigue, and hypokalemia
- Serious TRAEs occurred in 50% of patients
- None of the patients died while on study treatment or within 30 days of their last dose
- TEAEs led to dose delay of MIRV in 89% of patients; blurred vision led to dose delay in 28% of patients. TEAEs led to dose delay of carbo in 83% of patients
- TEAEs led to dose reduction of MIRV in 28% of patients. TEAEs led to dose reduction of carbo in 22% of patients
- Three patients (17%) discontinued MIRV due to TEAEs. Four patients (22%) discontinued carbo due to TEAEs

CONCLUSIONS

- MIRV + carbo shows promising antitumor activity in patients with platinum-sensitive ovarian cancer
- MIRV + carbo in the overall population resulted in an ORR of 71%, a mDOR of 12.1 months, and a mPFS of 16.4 months with 39% of patients having received 3+ prior therapies
- ORR, DOR, and PFS in this heavily pretreated, platinum-sensitive patient population compare favorably to historical phase 3 data in patients with fewer prior lines of therapy[9]
- MIRV 6 mg/kg AIBW + carbo AUC5 resulted in 89% ORR
- MIRV + carbo in patients with medium/high-FRα expression resulted in 80% ORR
- The safety profile of MIRV + carbo reflects the safety profile of each drug as monotherapy; the most common TRAEs were nausea, blurred vision, and thrombocytopenia

These findings support further evaluation of MIRV + carbo in patients with FRα-positive epithelial ovarian cancer (NCT05456685)

Abbreviations: ADC, antibody-drug conjugate; AE, adverse event; AIBW, adjusted ideal body weight; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AUC, area under the concentration-time curve; carbo, carboplatin; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EOC, epithelial ovarian cancer; FOLR1, folate receptor 1; FRα, folate receptor alpha; mDOR, median duration of response; MIRV, mirvetuximab soravtansine; mPFS, median progression-free survival; NE, not evaluable; ORR, objective response rate; PARP, poly (ADP-ribose) polymerase; PFS, progression-free survival; RECIST v1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; TEAEs, treatment-emergent adverse events; TRAEs, treatment-related adverse events.

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