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

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Abstract
Here we report the final safety and efficacy analysis of this combination regimen. Mirvetuximab soravtansine (MIRV) has shown clinically meaningful antitumor activity in patients with platinum-resistant ovarian cancer as a single agent and in combination therapy. As part of the phase 1/2 FORWARD trial (NCT03403452), MIRV combined with carboplatin (carbo) was evaluated in patients with recurrent folate receptor alpha-positive recurrent ovarian cancer. Here, we report the final safety and efficacy analysis of this combination regimen. The most common non-ocular treatment-related AEs were nausea, blurred vision, and neurotoxicity. The most common TRAEs were diarrhea, dry eye, and peripheral sensory neuropathy.

Methods (continued)
• This study enrolled adult patients with ≤3 lesions that met the definition of measurable disease according to RECIST v1.1 and PFS-positive (defined by immunohistochemistry with ≥25% of tumor cells with ≥2+ staining intensity).
• Patients received MIRV combined with carbo intravenously on day 1 of a 3-week cycle until disease progression, a starting dose of MIRV 6 mg/kg AIBW and carbo AUC4.
• Patients responded to platinum therapy and did not progress within 6 months of completing treatment.

Results: Efficacy
• The median DOR was 12.1 months (95% CI, 5.7–27.5) in the PS2 high subgroup (n=7).
• The median DOR was 12.1 months (95% CI, 3.7–27.5) in the subgroup with ≥50% of tumor cells with ≥2+ staining intensity.
• The median DOR was 24.2 months (95% CI, 6.1–25.0) in the subgroup with ≥25% of tumor cells with ≥2+ staining intensity.
• A total of 25% of tumor cells with ≥2+ staining intensity.

Baseline Demographics and Characteristics

<table>
<thead>
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<th>Primary diagnosis, n (%)</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platinum-sensitive ovarian cancer</td>
<td>18 (100)</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>

Median (range) duration of MIRV dosing
- MIRV 5 mg/kg ABIW + carbo AUC4: 9.5 months (4.0–14.1) (n=18)
- MIRV 5 mg/kg ABIW + carbo AUC3: 4.5 months (3.0–23.8) (n=9)
- MIRV 5 mg/kg ABIW + carbo AUC2: 6.2 months (2.7–14.0) (n=7)

Median (range) duration of carbo dosing
- MIRV 5 mg/kg ABIW + carbo AUC4: 7.9 months (2.7–23.5) (n=7)
- MIRV 5 mg/kg ABIW + carbo AUC3: 17.7 months (7.0–29.0) (n=7)
- MIRV 5 mg/kg ABIW + carbo AUC2: 14.5 months (9.0–22.0) (n=7)
- MIRV 6 mg/kg ABIW + carbo AUC2: 27.0 months (7.0–52.1) (n=7)

Results: Safety and Tolerability
- 79% (14/18) of patients continued in enrolled maintenance therapy. The most common non-ocular treatment-related AEs (TRAEs) were nausea, blurred vision, and neurotoxicity, and fatigue.
- Grade ≥3 TRAEs occurred in 56% of patients, the most common of which were neutropenia, thrombocytopenia, fatigue, and hypothyroidism.
- Serious TRAEs occurred in 52% 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 28% of patients; blurred vision led to dose delay in 26% of patients. TEAEs led to dose delay of carbo in 46% of patients.
- TEAEs led to dose reduction of MIRV in 28% of patients, blurred vision 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 efficacy evaluable patient group was 71% (12 of 17). Of those patients had a complete response, and 1 of 9 had a partial response (Figure 3).

- The DOR was 89% in patients receiving MIRV 6 mg/kg ABIW + carbo AUC2 (n=15), 44% of whom were classified as PS2 medium or high.
- The DOR was 83% in the medium-high-FR subgroup (n=10) and 37% in the low-FR subgroup (n=7).
- The median DOR was 12.1 months (95% CI, 3.7–27.5) in the subgroup with ≥50% of tumor cells with ≥2+ staining intensity.
- The median DOR was 12.1 months (95% CI, 4.4–18.1) in patients receiving MIRV 5 mg/kg ABIW + carbo AUC (n=8).
- The median DOR was 24.2 months (95% CI, 6.1–25.0) in the medium-high-FR subgroup (n=11) and low-FR subgroup (n=4) subgroups, respectively.
- The median PFS was 15.0 months (95% CI, 0.4–15.5) in the medium-high-FR subgroup (n=10) and 16.5 months (95% CI, 7.3–16.0) in the low-FR subgroup (n=7).

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 ovarian cancer (NCT05456685).