Mirvetuximab soravtansine, a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in combination with carboplatin and bevacizumab: final results from a Phase 1b study in patients (pts) with ovarian cancer

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Abstract

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INTRODUCTION

Advances in the treatment of platinum-sensitive disease with the introduction of PARP maintenance and bevacizumab combinations followed by daré have contributed to an increase in the prevalence of ovarian cancer.1 As the patient population expands, there is a need for additional, well-tolerated combinations in the platinum-sensitive setting. Bevacizumab is approved in combination with platinum-based doublets after initial surgical resection of advanced ovarian cancer and for platinum-sensitive disease that has recurred after 1 prior line of therapy.

For the carboplatin/gemcitabine/bevacizumab combination, the overall response rate (ORR) is 78% in post-platinum progression-free survival (PFS) of 12.4 months; for the carboplatin/paclitaxel/bevacizumab combination, the ORR is also 78% and PFS of 13.8 months.1, 2

Mirvetuximab soravtansine (MGS925) is an antibody-drug conjugate (ADC) comprising a folate receptor alpha (FRα)-binding antibody, cleavable linker, and the maytansinoid DM4, a potent tubulin-targeting agent. As monotherapy, mirvetuximab soravtansine has demonstrated impressive anti-tumor activity, along with a differentiated safety profile and favorable tolerability in FRα-positive platinum-resistant ovarian cancer.3

In separate combinations with carboplatin and with bevacizumab,4, 5 mirvetuximab soravtansine is well-tolerated, with promising anti-tumor activity. Here we report mature safety and efficacy findings from the phase 1b FORWARD II study (NCT02606305) evaluating the combination of mirvetuximab soravtansine with carboplatin and bevacizumab in patients with platinum-sensitive ovarian cancer.

Patient Population, Methods, and Objectives

Primary objective: Evaluate the safety, tolerability, and preliminary activity of mirvetuximab soravtansine when administered in combination with carboplatin and bevacizumab to patients with recurrent platinum-sensitive ovarian cancer.

Treatment schedule: Mirvetuximab soravtansine (6 mg/kg, adjusted ideal body weight) + carboplatin (AUC 5) + bevacizumab (15 mg/kg) administered on Day 1 of a 3-week cycle (Q3W); continuation of mirvetuximab soravtansine and bevacizumab as appropriate; Post-carboplatin (median 6 cycles), mirvetuximab soravtansine and bevacizumab continuation/maintenance is well tolerated

Eligibility:

• Platinum-sensitive EOC, primary peritoneal cancer, or fallopian tube cancer;
• Eligibility: FRα positivity by IHC (≥ 50% of tumor cells with ≥ 2+ staining intensity);
• Age: 18–80 years
• ECOG performance status (PS) 0–1
• No prior anti-angiogenic therapy

Endpoints:

• Primary endpoint: ORR
• Secondary endpoints: Median progression-free survival (PFS), median duration of response (DOR), median overall survival (OS), and safety profiles

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Results

Confirmed ORR and Time-to-Event Endpoints

No new safety signals were seen; adverse events observed with the triplet were as expected based on the side effect profiles of each agent and duration of therapy, with no new safety signals.

CONCLUSIONS

The combination of full-dose mirvetuximab soravtansine, carboplatin, and bevacizumab is well tolerated

No safety signals were seen; adverse events observed with the triplet were as expected based on the side effect profiles of each agent and duration of therapy, with no new safety signals.

Post-carboplatin (median 6 cycles), mirvetuximab soravtansine and bevacizumab continuation/maintenance is well tolerated

In patients with recurrent platinum-sensitive disease, the triplet shows encouraging clinical activity with an ORR of 83%, median DOR of 10.9 months and median PFS of 12 months.4

The efficacy outcomes observed with the MIRV triplet, in a heavily pretreated recurrent platinum sensitive population (27% had 2 priors, 24% had prior BEV, and 42% had prior PARPi), are encouraging relative to those reported in this setting, including the OCEANS and GOG 02303clinical studies.