Abstract 3592

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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INTRODUCTION

Advances in the treatment of platinum-sensitive disease with the introduction of targeted therapies including PARPi maintenance and bevacizumab combinations followed by bevacizumab maintenance have contributed to an increase in the prevalence of ovarian cancer.[1] As the patient population expands, there is a need for additional active, 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% and median progression free survival (mPFS) of 12.4 months; for the carboplatin/paclitaxel/bevacizumab combination, the ORR is also 78% and mPFS of 13.8 months. [2,3]

Mirvetuximab soravtansine (IMGN853) 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.[4]

In separate combinations with carboplatin[5] and with bevacizumab,[6] 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 maintenance therapy

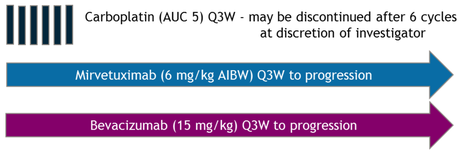
Eligibility:

- Platinum-sensitive EOC, primary peritoneal cancer, or fallopian tube cancer; defined as having not progressed within 6 months of last dose of platinum-containing therapy
- At least one lesion that met the definition of measurable disease (per RECIST 1.1)
- FRα positivity by IHC (≥ 50% of tumor cells with ≥ 2+ staining intensity)
- At least one, but not more than two, prior systemic treatment regimens
- Patients with history of bowel obstruction, abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess were excluded

Date of data cut: August 14, 2020

Dosing Schema and Summary of Drug Exposure

A



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No of Cycles Received	Carboplatin	Mirvetuximab soravtansine	Bevacizumab
Median (range)	6 (3-11)	12 (4-30)	13 (1-38)

Baseline Demographics

Characteristic	All Patients (n = 41)
Age	
Median (range)	63 (39-85)
Primary cancer diagnosis, *n (%)*	
Epithelial ovarian cancer	31 (76)
Fallopian tube cancer	9 (22)
Primary peritoneal cancer	1 (2)
ECOG PS, *n (%)*	
0	23 (56)
1	18 (44)
No. of prior systemic therapies, *n (%)*	
1	30 (73)
2*	11 (27)
Platinum-free treatment interval, *n (%)*	
≤ 12 months	22 (54)
> 12 months	19 (46)
FRα expression** *n (%)*	
High	20 (49)
Medium	21 (51)
Prior exposure, *n (%)*	
Platinum compounds	41 (100)
Taxanes	40 (98)
Bevacizumab	10 (24)
PARP inhibitor	17 (42)

** 1 patient had 3 priors
**PS2 scoring: High, ≥ 75% and medium, 50-74% of tumor cells with ≥ 2+ staining intensity

Treatment-Emergent Related^ Adverse Events >25% (n = 41)

Adverse Event	All Grades		Grade 3		Grade 4	
	No.	*%*	*No.*	*%*	*No.*	*%*
Diarrhea	34	83	4	10	0	0
Nausea	31	76	1	2	0	0
Fatigue	31	76	2	5	0	0
Thrombocytopenia	29	71	17	42	4	10
Vision blurred	28	68	0	0	0	0
Peripheral neuropathy†	23	56	0	0	0	0
Abdominal pain	20	49	0	0	0	0
Neutropenia	20	49	13	32	4	10
Keratopathy*	19	46	0	0	0	0
Vomiting	17	42	0	0	0	0
Dry eye	16	39	0	0	0	0
Decreased appetite	15	37	0	0	0	0
Headache	14	34	1	2	0	0
Anemia	13	32	5	12	0	0
AST increased	13	32	3	7	0	0
Hypertension	12	29	4	10	0	0

AST, aspartate aminotransferase
*Includes neuropathy peripheral, peripheral sensory neuropathy, paresthesia, and hypoesthesia
†Includes keratopathy, keratitis, corneal deposits, and corneal epithelial microcysts
^ Related to at least one drug

- 22 pts (54%) discontinued at least one drug due to treatment-related AEs
  - Primary carboplatin discontinuations occurred in 15 pts (37%) due to grade 2/3 thrombocytopenia
  - 13 pts (32%) discontinued mirvetuximab soravtansine due to a related AE (primarily thrombocytopenia [6 pts; 5 grade 2, 1 grade 3] or grade 2 blurred vision [2 pts])
  - 2 pts (5%) discontinued bevacizumab due to related AEs (grade 3 colonic fistula; grade 2 thrombocytopenia)
- Infusion-related reactions due to carboplatin seen in 5 pts (12%; 4 grade 2 and one grade 4 event)
- Two deaths on study or within 30 days of last dose, sepsis and acute respiratory failure, both considered not treatment-related

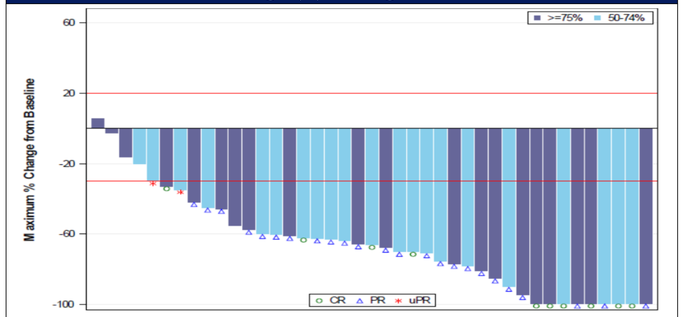
Confirmed ORR and Time-to-Event Endpoints

Endpoint	Total (n=41)	FRα Expression Medium (n=21)	FRα Expression High (n=20)
ORR (confirmed; 95% CI)	83% (68, 93)	86% (64, 97)	80% (56, 94)
DOR mo. (median; 95% CI)	10.9 (7.7, 13.6)	13.3 (6.7, 15.2)	9.9 (7.5, 12.3)
PFS mo. (median; 95% CI)	12.8 (9.1, 14.6)	12.9 (8.1, 16.2)	12.4 (9.0, 14.6)

DOR, duration of response; ND, not determined

- Pts (n=30) with 1 prior had an ORR of 90%, DOR of 9.7 mo. (7.6, 12.3) and PFS of 11.9 (9.0, 14.8)

Maximum Tumor Change (%) in Target Lesions from Baseline



CRs with <100% decrease: Lymph node target lesions that met CR definition per RECIST 1.1 (i.e. all pathological lymph nodes have reduction in short axis to <10 mm)
†Despite target lesion PR, overall response of patient at cycle 4 was PD due to appearance of new lesions

- Confirmed tumor responses were observed in 34 patients, consisting of 10 complete responses (CR) and 24 partial responses (PR); two additional patients had unconfirmed PRs as best response

CONCLUSIONS

- The combination of full dose mirvetuximab soravtansine, carboplatin, and bevacizumab is well tolerated
- 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 thrombocytopenia as the most common cause of drug-related discontinuations
- 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 12.8 months
- 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 GOG213[2,3] clinical studies

References:

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