Abstract 5547

Mirvetuximab soravtansine (IMGN853), a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC), in platinum-resistant epithelial ovarian cancer (EOC) patients: activity and safety analyses in Phase I pooled expansion cohorts

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INTRODUCTION

Elevated folate receptor alpha (FRα) expression is observed in approximately 80% of recurrent ovarian cancers, thus providing an attractive candidate for targeted therapeutic strategies in this indication

Mirvetuximab soravtansine (IMGN853) is an antibody-drug conjugate (ADC) comprised of a FRα-binding antibody, cleavable linker, and the maytansinoid DM4, a potent tubulin-targeting agent

The early clinical evaluation of mirvetuximab soravtansine has revealed good tolerability and encouraging activity when administered as monotherapy in patients with advanced EOC, particularly within the setting of platinum-resistant disease[1,2]

Primary or acquired resistance to platinum imparts a highly negative prognosis for EOC patients[3], and active agents in this population represent an urgent unmet medical need

Standard-of-care chemotherapeutics currently used as single agents in platinum-resistant disease (e.g. paclitaxel, pegylated liposomal doxorubicin, and topotecan) show low objective tumor response rates (15-20%) and progression-free survival (PFS; 3-4 months)[4-6]

A pooled analysis of safety and efficacy was performed in individuals with previously treated EOC, enrolled across three expansion cohorts as part of a Phase I trial of mirvetuximab soravtansine

This includes a subset of "FORWARD I eligible" patients who would have met the three key eligibility criteria for the recently initiated, pivotal Phase 3 study (FORWARD I; NCT02361876): platinum-resistant disease, medium/high FRα expression, and 1-3 prior lines of therapy

Objectives, Methods, and Patient Population

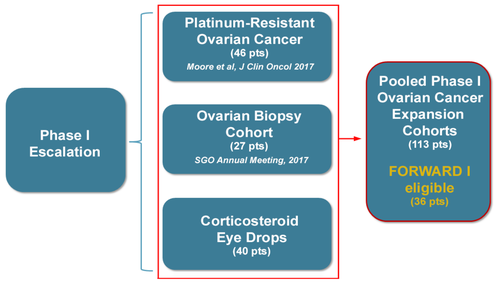
Primary objective: To characterize the safety and clinical activity of mirvetuximab soravtansine in a pooled analysis of EOC patients across three expansion cohorts

Treatment schedule: Mirvetuximab soravtansine administered at 6 mg/kg (AIBW) Q3W until disease progression, adverse event (AE), or investigator/patient decision

Key eligibility criteria for each expansion cohort:

- Platinum-resistant EOC cohort: Up to five prior lines of therapy, measurable disease
- Ovarian biopsy cohort: Recurrent disease, regardless of platinum sensitivity, and amenable to biopsy; measureable or non-measurable disease; no limit on number of prior lines of therapy
- Corticosteroid eye drop cohort: Recurrent disease, regardless of platinum sensitivity; measureable or non-measurable disease; 3-4 prior lines of therapy

Schema

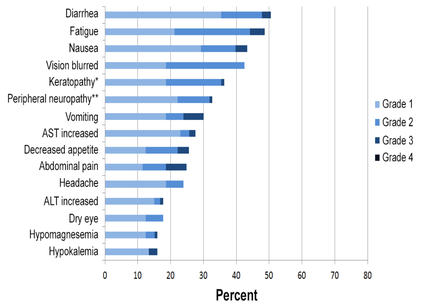


Baseline Demographics

	Pooled population (n = 113)	FORWARD I eligible (n = 36)
Age		
Median	61	65
Range	38-83	46-81
No. of prior systemic therapies		
Median	3	3
1-2	17 (15%)	10 (28%)
3	40 (35%)	26 (72%)
4+	56 (50%)	0 (0%)
Platinum Resistant		
Yes	96 (85%)	36 (100%)
No	17 (15%)	0 (0%)
Prior exposure		
Platinum compounds	113 (100%)	36 (100%)
Taxanes	113 (100%)	36 (100%)
Bevacizumab	76 (67%)	19 (53%)
PARP inhibitor	25 (22%)	7 (19%)
FRα expression*		
Low	23 (20%)	0 (0%)
Medium	29 (26%)	9 (25%)
High	61 (54%)	27 (75%)

*Low, 25-49%; Medium, 50-74%; High, ≥ 75% of tumor cells with 2+ staining intensity by IHC

Treatment Emergent AEs >15% (n = 113)



*Includes corneal cyst, corneal disorder, corneal deposits, corneal epithelial microcysts, keratitis, keratopathy, limbal stem cell deficiency, and punctate keratitis
**Includes neuropathy peripheral, peripheral sensory neuropathy, peripheral motor neuropathy, paresthesia, and hypoesthesia

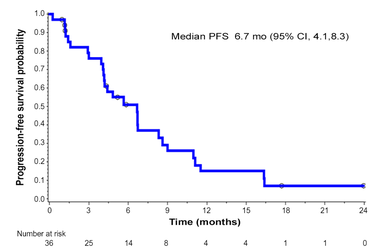
- Mirvetuximab was well tolerated across all ovarian cancer cohorts (n = 113)
- Adverse events were generally grade 1 or 2 and manageable
- No Grade ≥3 adverse event was present in ≥10% of patients
- The adverse event profile for the FORWARD I-eligible subset (n = 36) was consistent with the overall pooled population
- Drug-related AEs leading to discontinuation were seen in 10 patients (9%)

Confirmed ORR and Time to Event Endpoints

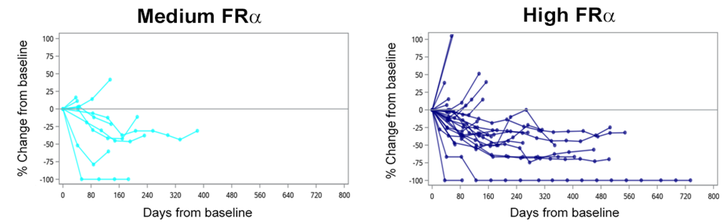
Endpoint	All Pooled Pts (n = 113)	FORWARD I eligible (n = 36)
ORR (confirmed) 95% CI	30%* (22, 39)	47%† (30, 65)
PFS (months) Median 95% CI	4.3 (3.9, 5.4)	6.7 (4.1, 8.3)
DOR (weeks) Median 95% CI	19.3 (18.0, 34.0)	25.1 (18.0, 42.0)

*3 complete responses (CR) and 31 partial responses (PR); †1 CR and 16 PR

Progression-Free Survival (FORWARD I eligible)



Percent Change in Tumor Target Lesions by FRα Expression (FORWARD I eligible)



Data are presented from 34/36 evaluable patients as target lesion measurements were not available for 2 individuals

CONCLUSIONS

- Mirvetuximab soravtansine demonstrates encouraging activity in platinum-resistant ovarian cancer
  - In FORWARD I eligible patients (platinum-resistant, 1-3 prior lines of therapy, and medium/high FRα expression) a confirmed ORR of 47% and median PFS of 6.7 months were achieved
- The Q3W dosing regimen continues to be well-tolerated, and the majority of adverse events were generally low grade and manageable
  - The discontinuation rate due to a related adverse event was 9%
- The consistency of data across cohorts supports the Phase 3 trial design
  - FORWARD I is the ongoing randomized Phase 3 study of mirvetuximab soravtansine monotherapy vs. investigator's choice chemotherapy, with PFS as the primary endpoint (ASCO Annual Meeting 2017, Abstract# TPS5607)

References: 1. K Moore et al. (2017) *J Clin Oncol* 35:1112-1118; 2. K Moore et al. (2017) Cancer doi:10.1002/cncr.3073; 3. A Davis et al. (2014) *Gynecol Oncol* 133:624-631; 4. D. Luvero et al. (2014) *Ther Adv Med Oncol* 6:229-239; 5. E Pujade-Lauraine et al. (2014) *J Clin Oncol* 32:1302-1308; 6. AM Poveda et al. (2015) *J Clin Oncol* 33:3836-3838.

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