Abstract 5567

IMGN853 (mirvetuximab soravtansine), a folate receptor alpha (FRα)-targeting antibody-drug conjugate (ADC): single agent activity in platinum-resistant epithelial ovarian cancer (EOC) patients

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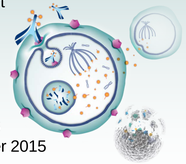
INTRODUCTION

- IMGN853 (mirvetuximab soravtansine) is an antibody-drug conjugate (ADC) comprising a folate receptor α (FRα)-binding antibody and the maytansinoid DM4, a potent tubulin-targeting agent
- In contrast to its restricted distribution in normal tissues, FRα is highly expressed in epithelial ovarian cancer (EOC), thus providing a rational therapeutic target for this malignancy
- IMGN853 is designed to bind surface-expressed FRα on cancer cells and be internalized; DM4 is then released through enzymatic degradation of the antibody and linker cleavage, enabling it to disrupt cell division and cause cell death via apoptosis
- Phase 1 dose finding identified a recommended phase 2 dose (RP2D) of 6.0 mg/kg adjusted ideal body weight (AIBW) IV Q3W (ASCO 2015, abstract 5558). Based on preliminary signs of efficacy seen during escalation, an expansion cohort was opened to assess this IMGN853 regimen in patients with platinum-resistant EOC
- A total of 46 patients were enrolled beginning in August 2014. We have previously reported interim findings for the initial 20 patients enrolled before April 2015 (ASCO 2015, abstract 5518); the final 26 patients were enrolled between April and September 2015



Patient Population, Methods & Objectives

Primary Objective: To understand the safety and clinical activity of IMGN853 in a FRα positive platinum-resistant EOC patient population

Secondary Objectives: To evaluate the tolerability of IMGN853 and to characterize its pharmacokinetics (PK) and immunogenicity

Treatment schedule: IMGN853 6.0 mg/kg AIBW IV Q3W until disease progression, AE or investigator/patient decision

Eligibility:

- Platinum-resistant EOC, primary peritoneal cancer or fallopian tube cancer
- Patients who had progressed or relapsed within 6 months of completing prior platinum-based therapy
- Patients with primary platinum-refractory disease are excluded
- Patients must have received no more than five prior systemic treatment regimens
- FRα positivity by IHC (≥25% of cells with 2+ intensity)

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For more information, please contact: scientificaffairs@immunogen.com

Baseline Demographics

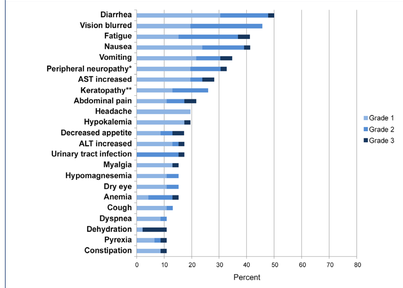
Characteristic	Patients (N = 46) No.	%
Age, years		
Median	62.5	
Range	41-81	
Sex		
Female	46	100
Race		
White	41	89
Black or African American	2	4
American Indian or Alaskan Native	2	4
Not reported	1	2
Primary diagnosis		
Epithelial ovarian cancer	40	87
Fallopian tube cancer	2	4
Primary peritoneal cancer	1	2
High grade Müllerian carcinoma	1	2
Serous and transitional cell carcinoma	1	2
Carcinosarcoma	1	2
ECOG PS		
0	22	48
1	24	52
No. of prior systemic therapies		
1 - 3	23	50
4+	23	50
Prior exposure		
Platinum compounds	46	100
Taxanes	46	100

Patient Disposition

Discontinued	44	96
Primary Reason for Discontinuation:		
Disease progression	32	70
Clinical progression	4	9
Withdrawal from study treatment	2	4
Adverse event*	5	11
Death**	1	2

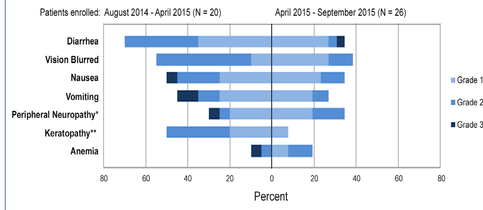
*Includes one patient who discontinued due to "other" – grade 3 hypersensitivity
**Small intestinal obstruction 2 months after single dose on day 1

Treatment Emergent AEs > 10% (n = 46)



*Includes Neuropathy peripheral, Peripheral sensory neuropathy, Peripheral motor neuropathy, Paraesthesia, and Hypoesthesia
**Includes Corneal cyst, Corneal disorder, Corneal deposits, Corneal epithelial microcysts, Keratitis, Keratopathy, Limbal stem cell deficiency, and Punctate keratitis

Comparison of Selected TEAEs



*Includes Neuropathy peripheral, Peripheral sensory neuropathy, Peripheral motor neuropathy, Paresthesia, and Hypoesthesia
**Includes Corneal cyst, Corneal disorder, Corneal deposits, Corneal epithelial microcysts, Keratitis, Keratopathy, Limbal stem cell deficiency, and Punctate keratitis

- Ocular adverse events, including blurred vision and keratopathy, decreased in both frequency and grade in the subset of 26 patients enrolled following the initial 20-patient cohort analyzed
  - This improvement may be due to the use of preservative-free lubricating eye drops and other measures mandated in April 2015 to manage such symptoms

Serious AEs and Dose Modifications

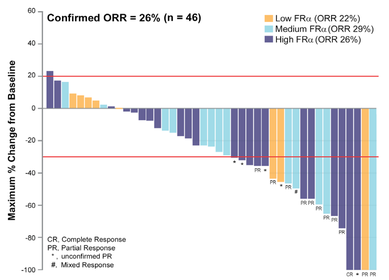
Drug-related Serious Adverse Events (SAEs):

- Occurred in 11 patients; no individual event was observed in more than one patient
- Three cases involved interstitial lung disease (1 each of Grade1 pulmonary fibrosis, Grade 2 pneumonitis, and Grade 2 organizing pneumonia)
- No Grade 5 events (deaths) were seen
- SAEs leading to discontinuation were:
  - Grade 2 pneumonitis
  - Grade 3 hypersensitivity
  - Grade 3 myelodysplastic syndrome
  - Grade 4 septic shock

Dose Modifications for Ocular Adverse Events:

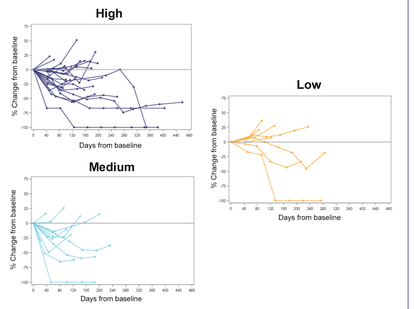
- 28% of patients (13/46) had at ≥ 1 dose delay or reduction for an ocular adverse event
  - 12 had at least one dose delay
  - 10 had at least one dose reduction; these took place in the 3rd cycle in 5 pts, 4th cycle in 4 pts, and 18th cycle for 1 pt
- 1 patient discontinued for grade 2 vision blurred with Grade 1 eye pain and corneal cyst

Maximum Percent Change in Target Lesions from Baseline



Note: Data is presented from 43 evaluable patients as post-baseline measurements were not available for 3 individuals.

Percent Tumor Change in Target Lesions by FRα Expression



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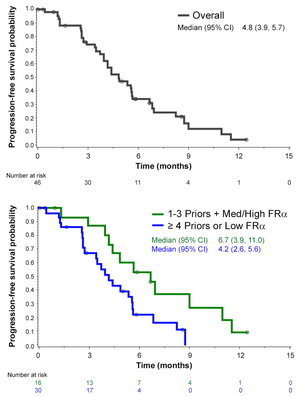
Confirmed ORR & Time to Event Endpoints by Prior Lines of Therapy

Endpoint	All pts (n = 46)	1-3 priors (n = 23)	1-3 priors + med/high FRα expression (n = 16)	≥ 4 priors or low FRα expression (n = 30)
ORR (%) 95% CI	26 (14, 41)	39 (20, 62)	44 (20, 70)	17 (6, 35)
PFS (months) Median 95% CI	4.8 (3.9, 5.7)	6.7 (3.9, 8.7)	6.7 (3.9, 11.0)	4.2 (2.6, 5.6)
DOR (weeks) Median 95% CI	19.1 (16.1, 33.1)	19.6 (17.7, 44.1)	26.1 (17.7, -)	19.1 (13.0, 20.1)

Progression-Free Survival



CONCLUSIONS

- IMGN853 demonstrates encouraging activity in platinum-resistant ovarian cancer, with a confirmed ORR of 26% (1 CR and 11 PRs) and a median PFS of 4.8 months for all evaluable patients (n = 46)
- Notably, the confirmed ORR was 44% in the subset of patients with 1-3 prior lines of therapy and medium/high FRα expression (n = 16), with a median PFS of 6.7 months
- Twenty-eight percent of patients required dose modifications due to low grade ocular AEs; in only one case was this a cause for discontinuation
  - Both blurred vision and keratopathy were decreased in those patients enrolled since April 2015, following implementation of more effective management procedures
  - An ongoing expansion cohort is exploring the use of primary prophylaxis with corticosteroid eye drops
- Based on the results of this study, the dose, schedule, and target population has now been identified for a pivotal Phase 3 trial of IMGN853 in patients with platinum-resistant ovarian cancer (FORWARD I)

The authors would like to especially thank the patients who have consented to be included in this study, as well as their families.
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