INTRODUCTION

IMGN853 (mirvetuximab soravtansine) is an antibody-drug conjugate (ADC) comprising a folate receptor alpha (FRα)-binding antibody and the maytansinoid DM4, a potent tubulin-targeting agent. FRα is overexpressed in epithelial ovarian cancer (EOC), thus providing a rational therapeutic target for this malignancy.

Patients with platinum-resistant EOC have options limited to single-agent chemotherapy. IMGN853 was 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.

In contrast to its restricted distribution in normal tissues, FRα is expressed in epithelial ovarian cancer, thus providing a rational therapeutic target for this malignancy.

METHODS

Eligibility:

- Patients must have received no more than five prior systemic treatments.
- Patients must have platinum-resistant EOC, primary peritoneal cancer or fallopian tube cancer.
- FRα positivity by IHC (≥25% of cells with 2+ intensity).
- Patients have evaluable disease on imaging.

A total of 46 patients were enrolled beginning in April 2015 (ASCO 2015, abstract 5518); the final 26 patients were enrolled between April and September 2015 (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 the 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.

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.
- Twenty-eight percent of patients required dose modifications due to low grade ocular AEs; in only one case was this a cause for discontinuation.
- IMGN853 shows promise for patients with 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.

严重的AEs and Dose Modifications

Drug-related Serious Adverse Events (SAEs):

- 28% of patients (13/46) had ≥1 dose delay or reduction for an ocular adverse event

Ocular 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 analysis.

This improvement may be due to the use of preservative-free lubricating eye drops and other measures implemented in April 2015 to manage such events.

Dose Modifications for Ocular Adverse Events:

- No Grade 5 events (deaths) were seen
- Three cases involved interstitial lung disease (1 each of Grade 1 pulmonary fibrosis, Grade 2 pneumonitis, and Grade 2 organizing pneumonia)
- 12 patients had at least one dose delay

Treatment emergent AEs >10% (n=46)

No grade 3 or 4 lab abnormalities were noted.

Percent Tumor Change in Target Lesions by FRα Expression

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