Characterization of folate receptor alpha (FRα) expression in archival tumor and biopsy samples in a Phase I study of mirvetuximab soravtansine (ADC), in relapsed epithelial ovarian cancer patients

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INTRODUCTION

- Mirvetuximab soravtansine (IMGN853) is an antibody-drug conjugate (ADC) comprising a folate receptor alpha (FRα)-binding antibody and the maytansinoid DM1, a potent tubulin-targeting agent
- FRα is highly expressed in epithelial ovarian cancer (EOC), thus providing a rational therapeutic target for this malignancy. Moreover, receptor expression is not altered by chemotherapy, further supporting a FRα-targeting strategy in the treatment of recurrent EOC1
- We have recently reported encouraging clinical activity and manageable safety for mirvetuximab soravtansine in EOC patients within the setting of platinum-resistant disease2
- Patient selection for clinical studies of mirvetuximab soravtansine is based on FRα positivity of archival tumor tissue
- As part of an ongoing Phase I trial (NCT01609556), an expansion cohort was opened in order to characterize FRα expression in archival and fresh biopsy samples (pre- and post-treatment) in patients with relapsed EOC
- A total of 27 heavily pre-treated individuals (up to 11 prior lines of therapy) were enrolled into this heterogeneous cohort of ovarian cancer patients, beginning in July 2015

Study Objectives:

- Characterize FRα expression in archival and pre- and post-treatment biopsy samples obtained from a heterogeneous cohort of relapsed EOC patients
- Determine concordance between archival and pre- and post-treatment FRα expression levels
- Compare FRα expression in pre-treatment versus post-treatment biopsy samples

Patient Population, Methods, and Biopsy Collection

- Treatment schedule:
  - Mirvetuximab soravtansine was administered intravenously at 6.0 mg/kg (adjusted ideal body weight) once every 3 weeks
- Eligibility:
  - ≥ 18 years of age
  - ≥ 11 prior lines of therapy
  - Eastern Cooperative Oncology Group (ECOG) status 0 to 2
  - Karnofsky Performance Status (KPS) ≥ 70
  - No prior exposure to anti-FOLR1 antibody or FRα-directed therapy
- Prior exposure:
  - Platinum compounds
  - Paclitaxel
  - Carboplatin
  - Bevacizumab
  - Bevacizumab-containing regimens
  - No limit on the number of prior treatment regimens

Biopsy collection:

- Core needle biopsy were collected before (baseline) and after (Cycle 2 Day 8) mirvetuximab soravtansine treatment
- FRα assay: anti-FOLR1 2.1 IMGN-generated antibody was used in an assay developed in collaboration with and validated at the Merck Institute for Medical Systems (Tucson, AZ), and run on a Benchmark XT IHC staining platform

Heterogeneous Patient Population

- The majority of AEs reported were grade 1 or 2
- 26% of patients (7/27) underwent one dose reduction due to an AE
- One patient discontinued for a related AE (organizing pneumonitis)

Effect of Archival and Pre-Treatment Biopsy Samples on FRα Expression

- Additional 3 patients remain on mirvetuximab soravtansine >12 months

Concordance of FRα Expression in Archival and Pre-Treatment Biopsy Samples

- 71% concordance of 23 evaluable pre-treatment samples, 15 met the eligibility criteria (> 25% cells with ≥ 2+ intensity)
- 76% of patients with the archival receptor level, two were subsequently shown to exceed 50% FRα positivity in their pre-treatment biopsy samples

- 22% of patients (6/27) did not have pre-treatment samples evaluable for FRα positivity due to insufficient tumor cell yield in the specimen
- 100% of archival samples provided sufficient tumor tissue for FRα testing

- Regardless of the tissue source analyzed (archival or pre-treatment biopsy), higher FRα expression is associated with greater antitumor activity

Measure of Clinical Activity Based on FRα Expression

- In this heavily pre-treated population, the confirmed objective response rate (ORR) was 22%, and the median progression-free survival (mPFS) was 4.2 months
- Two complete responses (CRs) were observed in individuals with high FRα expression
- Three patients remain on mirvetuximab soravtansine >12 months

CONCLUSIONS

- Concordance of FRα expression in pre-treatment biopsies versus archival tumor samples suggests that archival tissue may be reliably used to identify patients with receptor-positive tumors
- Archival tissue is appropriate for patient selection in mirvetuximab soravtansine clinical trials
- Fresh biopsy may be considered if archival tissue is not available if FRα levels are below eligibility criterion
- Matched pre- and post-treatment biopsies showed similar FRα expression levels following two doses of mirvetuximab soravtansine
- In this heterogeneous cohort of heavily pre-treated ovarian cancer patients, mirvetuximab soravtansine continues to demonstrate encouraging clinical activity and manageable safety
- Regardless of the tissue source analyzed (archival or biopsy), higher FRα expression is associated with greater antitumor activity
- These data support the use of archival tissue for patient selection in the recently initiated Phase 3 trial of mirvetuximab soravtansine (FORWARD 2; NCT02631767) in patients with platinum-resistant EOC, medium/high FRα expression, and 1-3 prior lines of therapy

References:


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