Mirvetuximab soravtansine (MIRV) is a first-in-class antibody-drug conjugate (ADC) comprising a folate receptor alpha (FRα) targeting agent. Clinical trials have demonstrated clinical activity with a favorable safety profile in patients with FRα-positive ovarian cancer.

Exposure Response (ER) Analysis for Efficacy and Safety of Mirvetuximab Soravtansine (MIRV) in Patients With Folate Receptor α (FRα)-Positive Cancer

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Methods

Clinical PK, efficacy, and safety data were collected from 541 patients in 3 clinical MIRV nano-liposomal therapy studies (IMGN853-0401, FORWARD I, and SORAYA).

Exposure endpoints evaluated in the ER analysis included ORR and PFS. ORR was defined in study protocols as the percentage of patients with a complete or partial response at the end of the study period. Tumor size was used as a surrogate efficacy endpoint in both MIRV monotherapy studies (IMGN853-0401, FORWARD I). Time-to-event endpoints included (censored) PFS and OS.

Continuous covariates: age, AIBW

– Dichotomous endpoints (ORR, AEs) were modeled using logistic regression. Time-to-event endpoints (PFS, OS) were modeled using a Cox proportional hazards model. A stepwise automated covariate model selection procedure was implemented, and a forward and backward stepwise elimination process was used to identify important exposure relationships and covariates.

Dichotomous endpoints (ORR, AEs) were evaluated using logistic regression. Time-to-event endpoints (PFS) were evaluated using Kaplan-Meier plots. The ER relationship was determined using Cox proportional hazard models. The overall interest in the ER model was determined using the likelihood ratio (LR) test (Figure 2).

Figure 2. IMGN853-0401 + FORWARD I Data Pool: Observed ORR in MIRV Exposure with Model Predicted Probability Density

Figure 3. SORAYA Data Pool: Effects of Exposure Metrics and Covariates on PFS

Figure 4. FORWARD I Data Pool: Effects of Exposure Metrics and Covariates on PFS

Figure 5. Observed AE (Grade ≥ 3) Occurrence vs MIRV AUC 0-d21 Model Based Predicted Probability Density

These data demonstrate the impact of MIRV exposure on both efficacy outcomes and the risk of AEs. Thus, highlighting the importance of adherence to recommended MIRV dosing guidelines in clinical practice.