**Population Pharmacokinetic (PK) Analysis of Mirvetuximab Soravtansine (MIRV) in Patients With Folate Receptor α (FRα)-Positive Cancer**

**Kathleen N. Moore,1 Domenica Lorasso,2 Ana Gakain,3 Sandro Pignata,4 Hanielore Denys,5 Niccolina Colombo,4 Toon Van Gorp,7 Jason A. Konner,8 Margarita Romeo,9 Philipp Harter,10 Conleth G. Murphy,11 Yaping Tu,12 Fengying Zhu,12 Brooke E. Bearer,13 Michael Michal,13 David J. Birrer,13 Robert L. Coleman,14 Ursula A. Matulonis,14 David M. O’Malley15

1Stephenson Cancer Center/Oklahoma University College of Medicine, Oklahoma City, Oklahoma, USA; 2Fondazione Policlinico Universitario IRCCS, Rome, Italy; 3Gynaecologic Cancer Programme, Vall d’Hebron Institute of Oncology (HIOH), Hospital Universitari Vall d’Hebron, Vall d’Hebron Barcelona Hospital Campus, Barcelona, Spain; 4IECC National Cancer Institute, Naples, Italy; 5Universitair Ziekenhuis Gent, Ghent, Belgium; 6Universidade Estadual de Ouro Preto, Ouro Preto, Minas Gerais, Brazil; 7Memorial Sloan Kettering Cancer Center, New York, New York, USA; 8KCI - Instituto Català d’Oncologia Badalona, Barcelona, Spain; 9Klinikum Essen-Eskele-Evans, Essen, Germany; 10Ron Sacks Kerr and Cancer Trials Ireland; 11ImmunoGen, Inc., Waltham, Massachusetts, USA; 12The Winthrop P. Rockefeller Cancer Institute at UAMS, Little Rock, Arkansas, USA; 13US Oncology Research, The Woodlands, Texas, USA; 14Dana-Farber Cancer Institute, Boston, Massachusetts, USA; 15Tamara CEE/Ohio State University Columbus, OHNS, USA

**BACKGROUND**

- Mirvetuximab soravtansine (MIRV) is a first-in-class antibody-drug conjugate (ADC) comprising a folate receptor alpha (FRα)-binding antibody, cleavable linker, and maytansinoid DM maytansine, a potent tubulin-targeting agent.
- MIRV has demonstrated clinically meaningful antitumor activity with a favorable safety profile in patients with FRα-positive ovarian cancer.3

A population PK (PopPK) model was developed to evaluate the effects of patient demographics and clinical characteristics on MIRV parameters.

We here report the results of the PopPK analyses of MIRV from 3 clinical studies (INGN555-0451 [phase 1]; FORWARD I [phase 3]; SORAYA [phase 3]).

**Objectives**

- Characterize the PK of MIRV in both single and multiple doses in patients with FRα-positive EOC.
- Explore the impact of patient demographics and clinical characteristics on relevant PK parameters.

**Methods**

- **Design**: A PopPK model was developed to determine the impact of patient demographics and clinical characteristics on evaluated PK parameters.
- **Data**: Data collected from the INGN555-0451 and FORWARD I trials were used to develop a base MIRV PopPK model, followed by a stepwise covariate search that identified statistically significant relationships.
- **MIRV PK parameters**: were optimized for a semi-mechanistic model. The final MIRV PopPK model was determined to be a 2-compartment model with both linear (non-specific) and nonlinear (target-mediated) elimination pathways for MIRV.

This model was then validated using data collected from the SORAYA study.

**Results: Statistically Significant Covariates**

- **Baseline demographics and clinical characteristics** were used as covariates in a stepwise covariate search that identified statistically significant relationships between:
  - AIBW: CL, V1, and V2
  - Age: CL and V2
  - Albumin: CL
  - AIBW, also known as AdjBW, is calculated as IBW (kg) + 0.4 (actual weight - IBW). IBW for females is calculated as 0.9*height (cm) –92.

**Results: Covariate Effects on MIRV Exposure**

- The final MIRV PopPK model included albumin on CL, V1, (Figure 1) and V2 as statistically significant covariates.

**Results: Covariate Effects on MIRV Exposure**

- Although AIBW demonstrated the largest effect on PK parameters, the impact of AIBW on MIRV exposure was negligible with 6 mg/kg MIRV dosing: AUC0–1h and Cmax,ss were predicted to vary by less than ±5% (Figure 3).
- Albumin had significant impact on CL but not on V1 or V2. Thus, variations in albumin were found to have a greater impact on AUC0–1h than on V1 or V2 (Figure 3).
- Variations in age had a minimal effect on AUC0–1h, and Cmax,ss were predicted to vary by less than ±5% (Figure 3).

**CONCLUSIONS**

- A PopPK model was developed to determine the impact of patient demographics and clinical characteristics on MIRV exposure.
- Covariates of statistical significance include AIBW, age, and albumin; however, the impact of these factors on evaluated PK parameters is negligible following 6 mg/kg MIRV dosing.
- Dosing adjustments do not appear to be necessary for patients with mild or moderate renal impairment or mild hepatic impairment.

This PopPK analysis supports the recommended dose of MIRV 6 mg/kg AIBW with MIRV exposure maintained within the target range for patients with FRα-positive ovarian cancer.