Abstract 1556

PICCOLO: An Open-Label, Single-Arm, Phase 2 Study of Mirvetuximab Soravtansine in Recurrent Platinum-Sensitive, High-Grade Epithelial Ovarian Cancers With High Folate Receptor Alpha (FRα) Expression

Angeles Alvarez Secord,[1] Sharyn Lewin,[2] Michael Method,[3] Sam-Mosley Ayuk,[3] Yuemei Wang,[3] Conleth G. Murphy,[4] Vanda Salutari,[5] Arantzazu Barquín,[6] Fernando Galvez,[7] Cara Mathews,[8] Ana Oaknin,[9] Maria Jesus Rubio,[10] Antonino Bonaventura,[11] Bradley Corr,[12] Sandro Pignata[13]

[1]Duke Cancer Institute, Durham, NC, USA; [2]Holy Name Medical Center, Teaneck, NJ, USA; [3]ImmunoGen, Inc., Waltham, MA, USA; [4]Bon Secours Cork and Cancer Trials Ireland; [5]Policlinico Universitario Fondazione Agostino Gemelli, IRCCS, Rome, Italy; [6]Hospital Universitario HM Sanchinarro, Madrid, Spain; [7]Hospital Universitario de Jaén, Jaén, Spain; [8]Women & Infants Hospital of Rhode Island, Providence, RI, USA; [9]Gynaecologic Cancer Programme, Vall d'Hebron Institute of Oncology (VHIO), Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; [10]Hospital Reina Sofía (Provincial), Córdoba, Spain; [11]Newcastle Private Hospital, New Lambton Heights, Australia; [12]University of Colorado School of Medicine, Aurora, CO, USA; [13]IRCCS Istituto Nazionale Tumori IRCCS-Fondazione G. Pascale, Naples, Italy

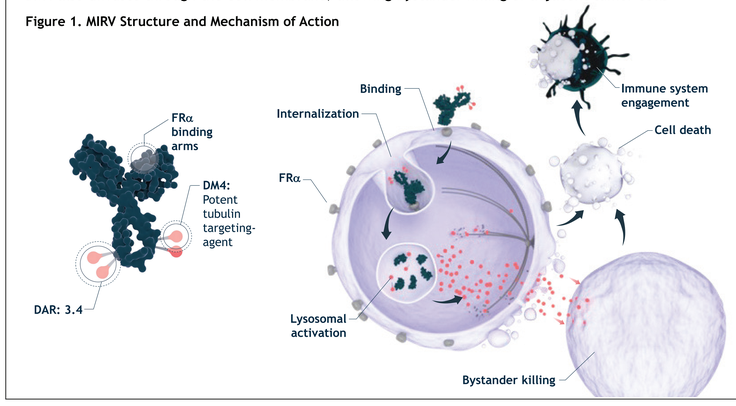
BACKGROUND

- Despite treatment advances for patients with recurrent platinum-sensitive ovarian cancer (PSOC), response rates and DOR are suboptimal, highlighting an unmet need[1]
- No standard of care exists for patients with PSOC who have been treated with multiple prior lines of therapy[2]
- Expression of folate receptor alpha (FRα) is limited on normal tissues but is elevated in most ovarian cancers, which makes FRα an attractive target for the development of novel therapies[3-5]
- Mirvetuximab soravtansine (MIRV) is an antibody-drug conjugate (ADC) comprising an FRα-binding antibody, a cleavable linker, and the maytansinoid DM4, a potent tubulin-targeting agent[6]
- Treatment with MIRV demonstrated clinically meaningful antitumor activity regardless of the number of prior lines of therapy or prior PARPi use[7,8]
  - SORAYA trial: Investigator-assessed ORR was 32.4% (95% CI, 23.6%–42.2%), including 5 CRs, and median DOR was 6.9 months[8]
  - FORWARD I trial: Investigator-assessed ORR was 38.0% (95% CI, 27.0%–49.0%) in FRα-high patients[9]
- Data from a subset of patients with PSOC and high FRα expression who received ≥2 prior lines of therapy, including prior MIRV experience (phase 1), showed an ORR of 64% (7 of 11 patients who achieved a response), including 2 CRs, each with a DOR of 15.7 months or longer[10]

Mechanism of Action

- The antibody portion of MIRV has been engineered to minimize its immunogenicity and binds to FRα on the surface of epithelial ovarian cancer (EOC) cells[2]
- MIRV is internalized via endocytosis[2]
- MIRV is degraded within the lysosome to release its cytotoxic payload (DM4)[2]
- The maytansine derivative DM4 disrupts tubulin, resulting in mitotic arrest and apoptosis; DM4 is 100- to 1000-fold more potent than vinca alkaloids[2]
- DM4 also diffuses through the cell membrane, allowing bystander killing of adjacent tumor cells[2]

Figure 1. MIRV Structure and Mechanism of Action



PICCOLO Trial Design

PICCOLO (NCT05041257) is a Single-arm, Phase 2, Global Study

Key Eligibility Criteria[11]

- Confirmed diagnosis of high-grade serous EOC, primary peritoneal cancer, or fallopian tube cancer
- Candidates for a nonplatinum, single-agent therapy as determined by the investigator
- Platinum-sensitive disease (platinum-free interval >6 months)
- Progressed radiographically on or after most recent line of anticancer therapy
- Received ≥2 prior lines of platinum-based therapy, or documented platinum allergy with 1 prior line of platinum-based therapy
- High FRα expression (≥75% of cells with PS2+ staining intensity as determined by immunohistochemistry)
  - The Ventana FOLR1 Assay will be used

Statistical Assumptions[11]

- Planned enrollment: N=75
- Null hypothesis: ORR is ≤28%; optimal Simon two-stage design without pause in enrollment

Mirvetuximab soravtansine

6 mg/kg AIBW[a] every 3 weeks intravenously

Primary Efficacy Endpoint[11]

- Investigator-assessed ORR, defined as confirmed best response of CR or PR

Key Secondary Endpoint[11]

- Investigator-assessed DOR, defined as the time from initial investigator-assessed response (CR or PR) until PD

Other Secondary Endpoints[11]

- Investigator-assessed PFS, defined as the time from first dose of MIRV until investigator-assessed radiological PD or death, whichever occurs first
- Overall survival, defined as the time from first dose of MIRV until death
- CA-125 response, determined using the Gynecologic Cancer Intergroup criteria
- Sensitivity analyses of ORR, DOR, and PFS by blinded independent central review
- Treatment-emergent adverse events, evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0

[a]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.

Additional Key Eligibility Criteria[11]

- ≥18 years of age
- Eastern Cooperative Oncology Group Performance Status of 0 or 1
- Testing for *BRCA* mutation (tumor or germline) and, if positive, must have received a prior PARPi as either treatment or maintenance therapy
- ≥1 lesion that meets the definition of measurable disease by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)
- Adequate hematologic, liver, and kidney functions

Key Exclusion Criteria[11]

- Endometrioid, clear cell, mucinous, or sarcomatous histology, mixed tumors containing any of the above histologies, or low-grade/borderline ovarian tumor
- Grade >1 peripheral neuropathy per CTCAE
- Active or chronic corneal disorders, history of corneal transplantation, or active ocular conditions requiring ongoing treatment/monitoring, such as uncontrolled glaucoma, wet age-related macular degeneration requiring intravitreal injections, active diabetic retinopathy with macular edema, macular degeneration, presence of papilledema, and/or monocular vision

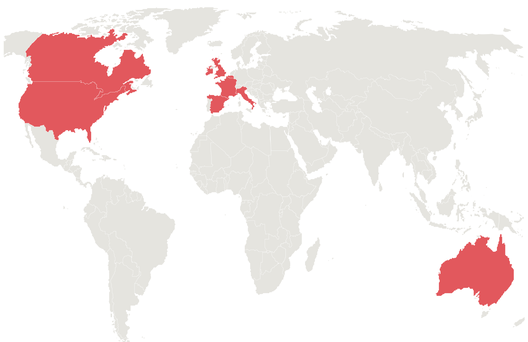
PICCOLO Trial Status

Overall Status and Enrollment

- This trial is in progress and enrolling globally[11]
- The first patient was enrolled in August 2021[11]

Trial Tracking Information

- This study is registered as ClinicalTrials.gov identifier: NCT05041257[11]



PICCOLO

Abbreviations: ADC, antibody-drug conjugate; AdjBW, adjusted body weight; AIBW, adjusted ideal body weight; *BRCA*, BReast CAncer gene; CA-125, cancer antigen 125; CRs, complete responses; CTCAE, Common Terminology Criteria for Adverse Events; DAR, drug to antibody ratio; DM4, N2′-[4-[(3-carboxypropyl)dithio]-4-methyl-1-oxo-2-sulfopentyl]-N2′-deacetylmaytansine; DOR, duration of response; EOC, epithelial ovarian cancer; FRα, folate receptor alpha; IBW, ideal body weight; MIRV, mirvetuximab soravtansine; ORR, objective response rate; PARPi, poly (adenosine diphosphate [ADP]-ribose) polymerase inhibitor; PD, progressive disease; PFS, progression-free survival; PR, partial response; PSOC, platinum-sensitive ovarian cancer; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

Acknowledgements: The authors would like to especially thank the patients who consented to be included in these trials, as well as their families. Editorial assistance and writing support in the preparation of this poster were provided by PRECISIONscientia, funded by ImmunoGen, Inc. Studies described here were sponsored by ImmunoGen, Inc.

References: **1.** Buechel M, et al. *Ann Oncol*. 2019;30(5):721-732. **2.** Secord AA, et al. Poster presented at: SGO Annual Meeting on Women's Cancer; March 18-21, 2022; Phoenix, AZ. **3.** Crane LMA, et al. *Cell Oncol (Dordr)*. 2012;35(1):9-18. **4.** Kalli KR, et al. *Gynecol Oncol*. 2008;108(3):619-626. **5.** Chen Y-L, et al. *Mol Oncol*. 2012;6(3):360-369. **6.** Moore KN, et al. *Cancer*. 2017;123(16):3080-3087. **7.** Matulonis UA, et al. Presented at: SGO 2022 Annual Meeting on Women's Cancer; March 18-21, 2022; Phoenix, AZ. **8.** Matulonis UA, et al. Poster presented at: 2022 ASCO Annual Meeting; June 3-7, 2022; Chicago, IL. **9.** Moore KN, et al. Presented at: ESMO Congress 2019; September 27-October 1, 2019; Barcelona, Spain. **10.** Data on file. ImmunoGen, Inc., 2022. **11.** ClinicalTrials.gov identifier: NCT05041257. Updated July 27, 2022. Accessed August 29, 2022. https://clinicaltrials.gov/ct2/show/NCT05041257.