ARTISTRY-7: Phase 3, Multicenter Study of Nemvaleukin Alfa Plus Pembrolizumab Versus Chemotherapy in Patients With Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (GOG-3063; ENGOT-OV68)

Poster # TPS5609

Thomas J. Herzog,[1] Kathleen Moore,[2] Panagiotis A. Konstantinopoulos,[3] Lucy Gilbert,[4] John L. Hays,[5] Bradley J. Monk,[6] David M. O'Malley,[7] Jalid Sehouli,[8] Joyce N. Barlin,[9] Julie R. Graham,[10] Monali Desai,[10] Yan Wang,[10] Yangchun Du,[10] Rita Dalal,[10] Robert L. Coleman[11]

[1]UC Cancer Center College of Medicine, University of Cincinnati, Cincinnati, OH; [2]Stephenson Cancer Center, University of Oklahoma Health Sciences Center, Oklahoma City, OK; [3]Dana-Farber Cancer Institute, Boston, MA; [4]McGill University Health Centre, Woman's Health Research Unit, Montréal, QC, Canada; [5]Wexner Medical Center and James Cancer Hospital, Ohio State University, Columbus, OH; [6]Arizona Oncology, University of Arizona College of Medicine, Creighton University School of Medicine, Phoenix, AZ; [7]The James Gynecologic Oncology Mill Run, Ohio State University, Hillard, OH; [8]Charité Universitaetsmedizin Berlin Charité Campus Virchow-Klinikum, Berlin, Germany; [9]Women's Cancer Care Associates, Albany, NY; [10]Alkermes, Inc., Waltham, MA; [11]Texas Oncology, The Woodlands, TX

INTRODUCTION

Nemvaleukin is a novel, engineered cytokine under evaluation for the treatment of platinum-resistant ovarian cancer (PROC)

- Despite the initial success of standard frontline platinum-based chemotherapy in the treatment of ovarian cancer (OC), 70% of women will have recurrent disease within 2 years[1]
- Interleukin-2 (IL-2) has both immunosuppressive and immunostimulatory functions, mediated by its interaction with different IL-2 receptor (IL-2R) complexes (Figure 1)[2]
- Nemvaleukin is an engineered cytokine designed to selectively bind to the intermediate-affinity IL-2R for preferential activation and expansion of tumor-killing CD8+ T cells and natural killer (NK) cells, with minimal expansion of regulatory T cells (T_{regs}), as well as mitigation of toxicities associated with high-dose IL-2 (Figure 2)[2]

Figure 1: Cell activation by IL-2

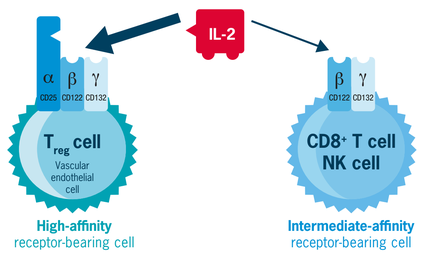
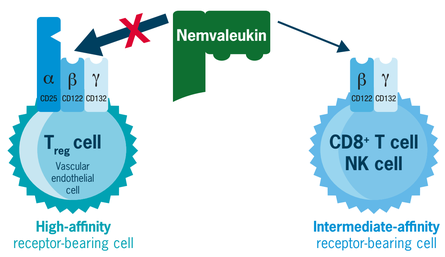


Figure 2: Nemvaleukin is a stable fusion of IL-2 and IL-2Rα



IL-2

- Preferential activation of high-affinity IL-2R by high-dose IL-2 leads to expansion of T_{regs}, which may counteract antitumor activity as well as stimulate vascular endothelial cells
- Activation of vascular endothelial cells is associated with high incidence of acute toxicities, including capillary leak syndrome

Nemvaleukin

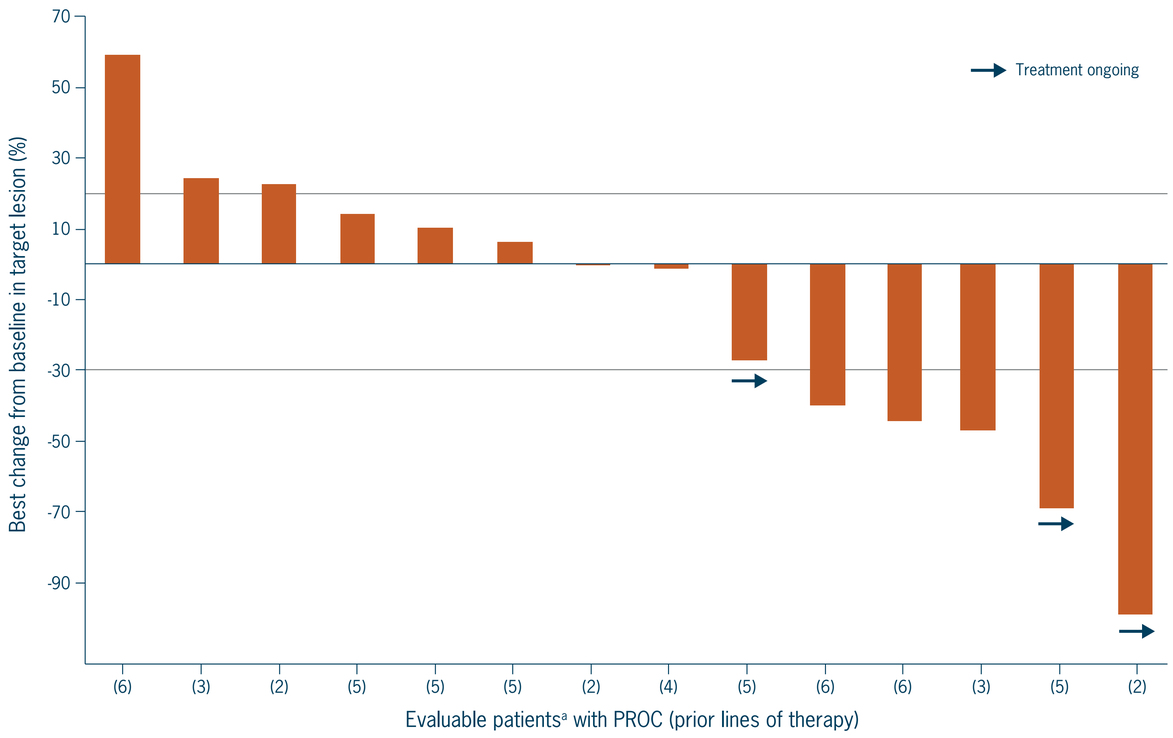
- Stable fusion protein designed to harness the validated IL-2 pathway biology
- Intrinsically active immediately upon systemic entry; does not degrade into native IL-2
- Designed to selectively bind the intermediate-affinity IL-2R to:
  - Preferentially activate memory cytotoxic CD8+ T cells and NK cells without expanding CD4+ T_{regs}
  - Mitigate toxicities associated with preferential binding of IL-2 to high-affinity IL-2R
- Leads to increases in both peripheral and intratumoral immune effector cells

Clinical and preclinical nemvaleukin studies have shown responses across a broad range of tumor types, including in OC

- In clinical studies, responses to nemvaleukin, as monotherapy and in combination with pembrolizumab, were observed in various tumor types, including breast, cervical, head and neck, gastrointestinal, genitourinary, lung, and PROC (see Figure 3 for responses to combination therapy in PROC [n=15, 14 evaluable patients, 2-6 prior lines of therapy])[3-6]
  - Monotherapy: objective responses in 4 patients with renal cell carcinoma (1 unconfirmed), 2 with mucosal melanoma (1 unconfirmed), and 2 with cutaneous melanoma (1 unconfirmed; 1 confirmed with 4 prior lines of therapy)[3,6]
  - Combination: objective responses in 22 patients; 5 heavily pretreated (range, 4-8 prior lines of therapy)[4,6]
- Nemvaleukin was generally well tolerated and did not demonstrate any additive toxicity to that already established with pembrolizumab alone[4]
- Nemvaleukin in combination with pembrolizumab has been granted Fast Track designation for the treatment of PROC by the US Food and Drug Administration
- **Here we describe the actively recruiting, phase 3 ARTISTRY-7 study of nemvaleukin plus pembrolizumab in platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer (NCT05092360)**

Figure 3: ARTISTRY-1 best change from baseline in sum of target lesions with nemvaleukin plus pembrolizumab in patients with PROC

(See Vaishampayan et al. Abstract #2500 [oral presentation] at this congress)



[a]N=14 evaluable patients with PROC who received nemvaleukin 3 µg/kg IV + pembrolizumab and ≥1 postbaseline scan.
Response per Response Evaluation Criteria In Solid Tumors (RECIST) v1.1. Data cutoff October 29, 2021.
IV, intravenous.

ARTISTRY-7 (GOG-3063; ENGOT-OV68; NCT05092360) STUDY DESIGN

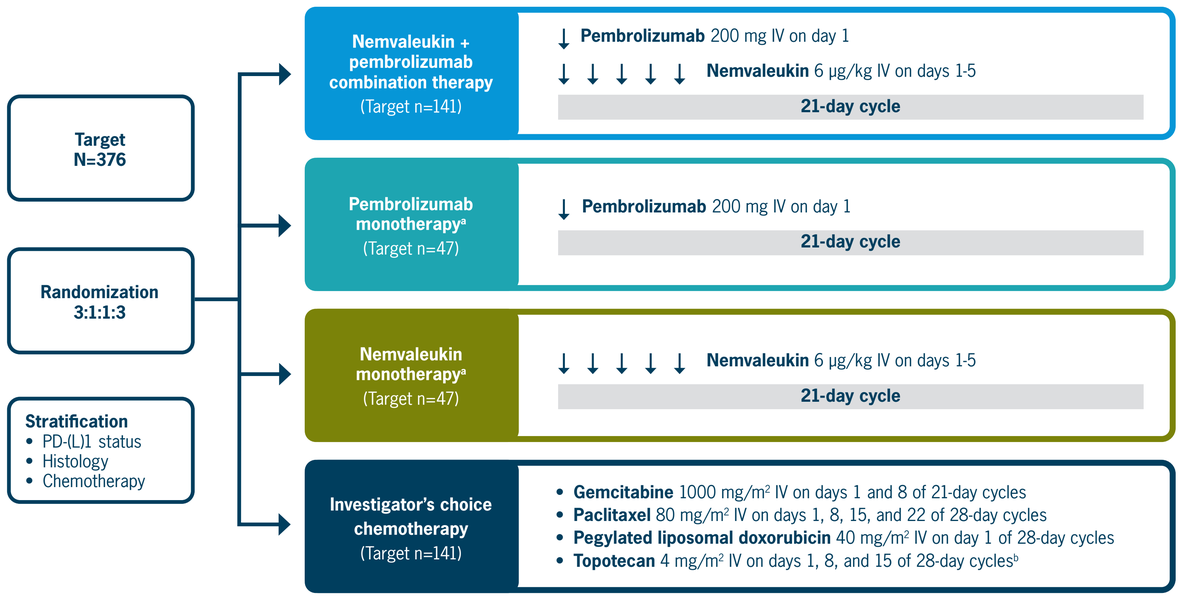
ARTISTRY-7: Global trial; 110 sites in 17 countries

Key inclusion criteria

- Women aged ≥18 years with platinum-resistant epithelial OC (high-grade serous, endometrioid, clear cell), fallopian tube cancer, or primary peritoneal cancer
- Must have received:
  - ≥1 prior line of systemic anticancer therapy in the platinum-sensitive setting
  - ≤5 prior lines of therapy in the platinum-resistant setting
  - Prior bevacizumab
  - Prior PARP inhibitor for patients with *BRCA* mutation
- Evidence of radiographic progression on or after most recent therapy
- Eastern Cooperative Oncology Group performance status of 0 or 1
- Estimated life expectancy of ≥3 months
- Adequate hematologic reserve and hepatic and renal function

Key exclusion criteria

- Primary platinum-refractory disease (progression during first-line platinum-based therapy)
- Primary platinum resistance (progression <3 months after completion of first-line platinum-based therapy)
- Prior programmed death (ligand) 1 (PD-[L]1) therapy
- Prior IL-2, IL-15, or IL-12 therapy
- Epithelial OC with mucinous or carcinosarcoma subtype, nonepithelial tumors
- Fluid drainage (eg, paracentesis, thoracentesis, pericardiocentesis) of ≥500 mL within 6 weeks of study drug initiation



[a]Futility analyses planned to stop the monotherapy arms earlier. [b]1.25 mg/m² on days 1-5 of 21-day cycles is also an option.

- Patients will continue treatment in the absence of disease progression or intolerable toxicity (maximum 35 cycles for pembrolizumab; nemvaleukin can be continued)
- Patients will be followed for survival beyond treatment discontinuation

Primary endpoint

- Investigator-assessed progression-free survival (RECIST v1.1) in patients treated with nemvaleukin plus pembrolizumab versus chemotherapy

Secondary/Exploratory endpoints

- Characterization of antitumor activity (objective response rate, overall survival, disease control rate, duration of response, and time to response) of nemvaleukin and pembrolizumab in combination and as monotherapy
- Safety, health-related quality of life, pharmacokinetic/pharmacodynamic effects

REFERENCES AND ACKNOWLEDGMENTS

References

1. Dion L, et al. *J Clin Med*. 2020;9:2239.
2. Lopes JE, et al. *J Immunother Cancer*. 2020;8(1):e000673.
3. Lewis K, et al. Poster presented at Melanoma Bridge 2021.
4. Boni V, et al. *J Clin Oncol*. 2021;39(suppl 15): Abstract #2513.
5. Hamid O, et al. *J Clin Oncol*. 2021;39(suppl 15): Abstract #2552.
6. Data on file. Alkermes, Inc.

Acknowledgments

The authors would like to thank all the patients who are participating in this study and their families.
This study is sponsored by Alkermes, Inc., and conducted in collaboration with Merck, Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; the Gynecologic Oncology Group (GOG); and European Network of Gynaecological Oncological Trial groups (ENGOT).
Medical writing and editorial support was provided by Parexel and funded by Alkermes, Inc.

Contact: USMedInfo@Alkermes.com

GOG Gynecologic Oncology Group
ENGOT European Network of Gynaecological Oncological Trial groups
ARTISTRY

ClinicalTrials.gov ID: NCT05092360