Society of Gynecologic Oncology
ANNUAL MEETING ON WOMENS' CANCER®
BUILDING BRIDGES // BREAKING BARRIERS
SGO // PHOENIX, ARIZONA // MARCH 18 – 21, 2022

ARTISTRY-7: a Phase 3, Multicenter Study of Nemvaleukin Alfa, a Novel Engineered Cytokine, in Combination With Pembrolizumab Versus Chemotherapy in Patients With Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

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INTRODUCTION

Nemvaleukin Is a Novel, Engineered Cytokine Under Evaluation in Platinum-Resistant Ovarian Cancer (OC)

- Despite the initial success of standard frontline platinum-based chemotherapy in the treatment of OC, 70% of women will have recurrent disease within 2 years of this treatment.[1]
- Nemvaleukin is an engineered cytokine designed to selectively bind to the intermediate-affinity interleukin-2 receptor (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 1).[2]
- IL-2 has both immunosuppressive and immunostimulatory functions, mediated by its interaction with different IL-2R complexes (Figure 2).[2]

Figure 1: Nemvaleukin Is a Stable Fusion of IL-2 and IL-2Rα

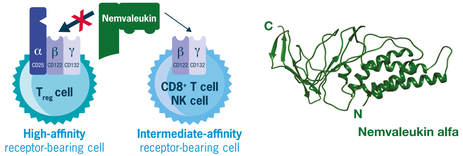
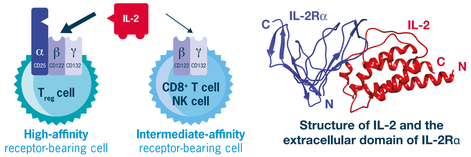


Figure 2: Cell Activation by IL-2



Nemvaleukin
- Nemvaleukin was engineered using native IL-2 and the extracellular region of the IL-2Rα domain
- Stable fusion protein that is intrinsically active immediately upon systemic entry[1]
- Does not require metabolic activation or degrade to native IL-2[1]
- Sterically occluded from binding to the high-affinity IL-2R[1]

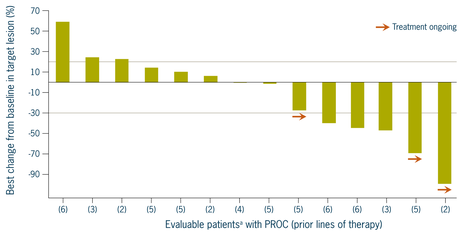
IL-2
- Potently activates the high-affinity IL-2R, which is preferentially expressed on immunosuppressive T_{regs} and vascular endothelial cells[1]
- Preferential binding of high-affinity IL-2R by high-dose IL-2 leads to expansion of T_{regs},[4] which may counteract antitumor activity as well as stimulate vascular endothelial cells, which can upregulate the high-affinity IL-2R and are associated with severe toxicities, including capillary leak syndrome[1]

Clinical and Preclinical Nemvaleukin Studies Have Shown Responses Across a Broad Range of Tumor Types, Including in OC

- Antitumor activity of multiple agents (ie, chemotherapy, checkpoint inhibitors, and tyrosine kinase inhibitors) was enhanced in combination with nemvaleukin in preclinical studies.[3-5]
- 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 platinum-resistant OC (see Figure 3 for responses to combination therapy in platinum-resistant OC [n = 15, 14 evaluable patients, 2-6 prior lines of therapy]).[6-9]
  - 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).[6,9]
  - Combination: objective responses in 22 patients; 5 heavily pretreated (range, 4-8 prior lines of therapy).[7,9]
- The observed safety profile of nemvaleukin to date is consistent with that anticipated from its design.[6-8] Moreover, nemvaleukin did not demonstrate any additive toxicity to that already established with pembrolizumab alone.[7]
- Nemvaleukin in combination with pembrolizumab has been granted Fast Track designation for the treatment of platinum-resistant OC by the US FDA.
- **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 Percent Change in Tumor Size Among 15 Patients With Platinum-Resistant Ovarian Cancer

(See Abstract 11982 [oral presentation] at this congress by Winer et al.)



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

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

Key Inclusion Criteria
- Females 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 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, and 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

Target N = 376

Randomization 3:1:1:3

Nemvaleukin + pembrolizumab combination therapy (Target n = 141)	↓ **Pembrolizumab** (200 mg IV) on day 1 ↓ ↓ ↓ ↓ ↓ **Nemvaleukin** (6 µg/kg IV) on days 1-5 **21-day cycle**
Nemvaleukin monotherapy[a] (Target n = 47)	↓ ↓ ↓ ↓ ↓ **Nemvaleukin** (6 µg/kg IV) on days 1-5 **21-day cycle**
Pembrolizumab monotherapy[a] (Target n = 47)	↓ **Pembrolizumab** (200 mg IV) on day 1 **21-day cycle**
Investigator's choice chemotherapy (Target n = 141)	• **Gemcitabine** (1000 mg/m² IV) on days 1 and 8 of 21-day cycles • **Paclitaxel** (80 mg/m² IV) on days 1, 8, 15, and 22 of 28-day cycles • **Pegylated liposomal doxorubicin** (40 mg/m² IV) on day 1 of 28-day cycles • **Topotecan** (4 mg/m² IV) on days 1, 8, and 15 of 28-day cycles[b]

[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.

Primary Endpoint
- Investigator-assessed progression-free survival (RECIST v1.1) in patients treated with nemvaleukin plus pembrolizumab vs 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

Treatment Groups

- Patients will be stratified according to PD-L1 status, histologic subtype, and chemotherapy.
- 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.

ARTISTRY-7 (NCT05092360) Global Study: Targeted Countries

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.

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. Losey HC, et al. Poster presented at AACR 2017; Abstract #591.
4. Lopes JE, et al. Poster presented at AACR 2020; Abstract #2202.
5. Pan Y, et al. Poster presented at ESMO 2021; Abstract #3326.
6. Lewis K, et al. Poster presented at Melanoma Bridge 2021.
7. Boni V, et al. *J Clin Oncol.* 2021;39(suppl 15): Abstract #2513.
8. Hamid O, et al. *J Clin Oncol.* 2021;39(suppl 15): Abstract #2552.
9. Data on file. Alkermes, Inc.