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)

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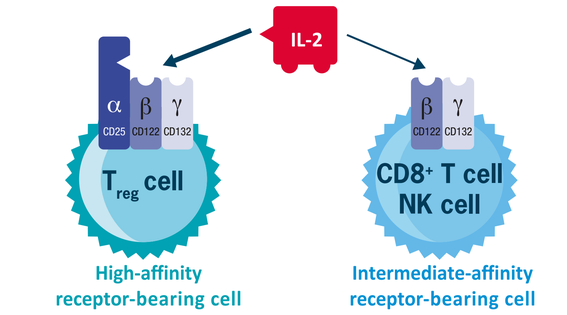
INTRODUCTION

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]
- In the platinum-resistant setting, standard-of-care chemotherapy and anti–programmed cell death 1 (anti-PD1) therapy in clinical trials have modest response rates ranging from ~6% to 20% and ~7% to 12%, respectively[2-6]
- Interleukin-2 (IL-2) has both immunosuppressive and immunostimulatory functions, mediated by its interaction with different IL-2 receptor (IL-2R) complexes (Figure 1)[7]
- 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}), while mitigating toxicities associated with high-dose IL-2 (Figure 2)[7]

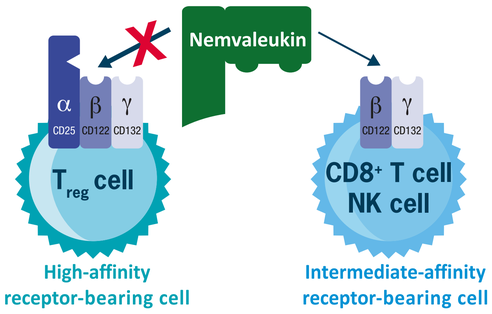
Figure 1: Cell activation by IL-2



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 a high incidence of acute toxicities, including capillary leak syndrome

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



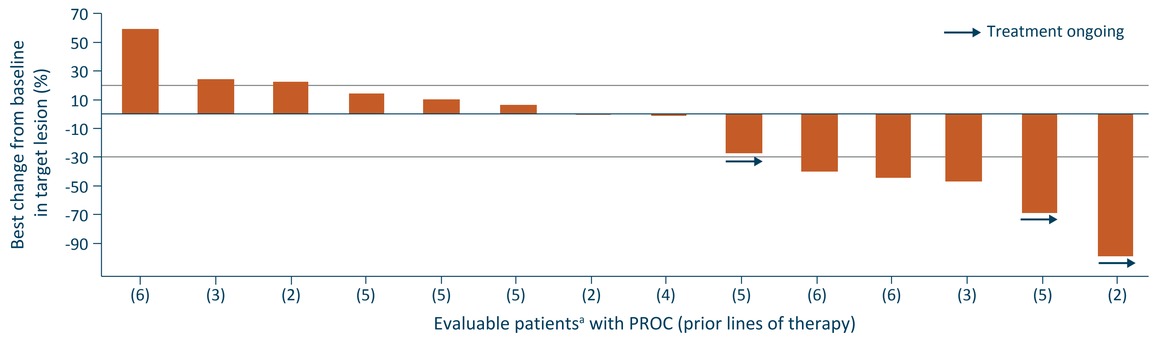
Nemvaleukin

- Stable fusion protein; intrinsically active upon systemic entry; does not degrade into native IL-2
- Designed to harness the validated IL-2 pathway biology
- 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])[8-11]
  - Monotherapy: objective responses in 4 patients with renal cell carcinoma (1 unconfirmed), 2 with mucosal melanoma (1 unconfirmed), and 4 with cutaneous melanoma (1 unconfirmed; 1 awaiting confirmation [occurred after data cutoff date])[8,11]
  - Combination: objective responses in 22 patients; 5 heavily pretreated (range, 4-8 prior lines of therapy)[9,11]
  - Combination (PROC): 4 responses, including 2 complete and 2 partial responses (1 unconfirmed); objective response rate (ORR) 28.6%; disease control rate (DCR) 71.4%; median duration of response (DOR) 53.4 weeks[11]
- Nemvaleukin was generally well tolerated and did not demonstrate any additive toxicity to that already established with pembrolizumab alone[9]
- 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



[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 v1.1. Data cutoff October 29, 2021.
IV, intravenous.

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

ARTISTRY-7: Global trial in 19 countries; recruitment in this trial is ongoing

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 platinum-based therapy[a]
  - ≤5 prior lines of systemic anticancer 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

[a]Patients who received only 1 prior line of platinum-based therapy must have received ≥4 cycles, have had a complete or partial response, and then progressed ≥3 or ≤6 months after the last dose.

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 4 weeks of study drug initiation

Target
N=376

Randomization
3:1:1:3

Stratification
- PD-(L)1 status
- Histology
- Chemotherapy

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**
Pembrolizumab monotherapy[a] (Target n=47)	↓ **Pembrolizumab** 200 mg IV on day 1 **21-day cycle**
Nemvaleukin monotherapy[a] (Target n=47)	↓ ↓ ↓ ↓ ↓ **Nemvaleukin** 6 µg/kg IV on days 1-5 **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.

- Patients will continue treatment in the absence of disease progression or intolerable toxicity (maximum 35 cycles for pembrolizumab; nemvaleukin can be continued)
- Patient survival will be followed until study end or up to 3 years after initiation of treatment, whichever occurs first

Primary endpoint

- Investigator-assessed progression-free survival (Response Evaluation Criteria In Solid Tumors v1.1) in patients treated with nemvaleukin plus pembrolizumab versus chemotherapy

Secondary/Exploratory endpoints

- Characterization of antitumor activity (ORR, overall survival, DCR, DOR, and time to response) of nemvaleukin and pembrolizumab in combination and as monotherapy
- Safety, health-related quality of life, pharmacokinetic/pharmacodynamic effects

ARTISTRY-7 (NCT05092360) Global Study: Targeted Countries

ARTISTRY
ClinicalTrials.gov ID:
NCT05092360

Gynecologic Oncology Group

ENGOT
European Network of Gynaecological Oncological Trial groups

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