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Clinical outcomes of ovarian cancer patients treated with the novel engineered cytokine nemvaleukin alfa in combination with the PD-1 inhibitor pembrolizumab: recent data from ARTISTRY-1

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*At the time of the study

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Financial Disclosures

- I have no financial relationships with ACCME defined ineligible companies to report over the past 24 months

Unlabeled/Investigational Uses

- I will be discussing unlabeled or investigational use of a pharmaceutical product, namely, nemvaleukin, in combination with pembrolizumab for the treatment of patients with ovarian cancer

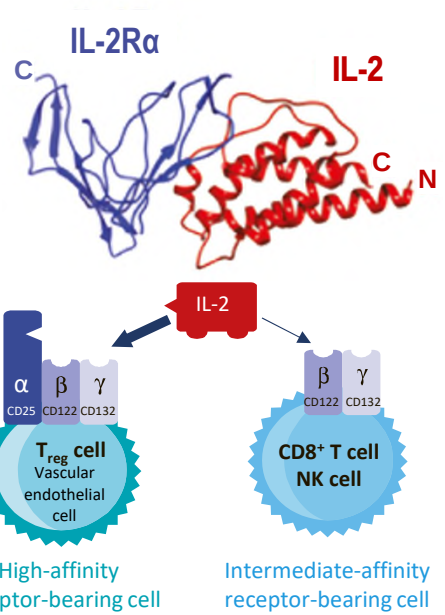
Unmet medical need for patients with PROC

- Most patients have advanced disease at diagnosis[1-3] and undergo surgery followed by platinum-based chemotherapy[3,4]
- Many tumors become resistant to or are refractory to platinum-based chemotherapy; prognosis is poor for patients with PROC[3-5]
- Ovarian cancer does not typically respond to single-agent checkpoint inhibitor therapy[5]
- Median progression-free survival for patients is ~3.5 months with systemic chemotherapy regimens[6]

PROC, platinum-resistant ovarian cancer.

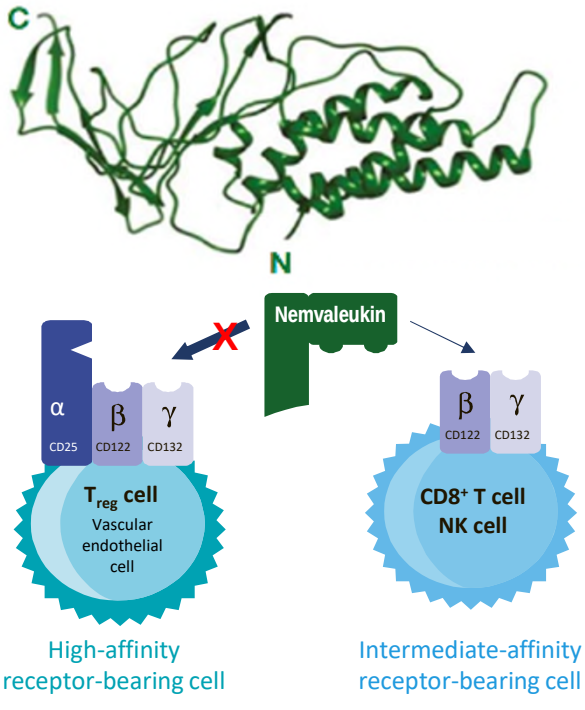
1. Torre LA, et al. *CA Cancer J Clin.* 2018; 68:284-296. 2. Dion L, et al. *J Clin Med* 2020;9:2239. 3. Kurnit KC, et al. *Obstet Gynecol.* 2021;137:108-121. 4. NCCN Ovarian Cancer Version 3.2021 – September 9, 2021. 5. Palai I, et al. *OncoTargets Ther.* 2020:13 6109-6129. 6. Pujade-Lauraine E, et al. *J Clin Oncol.* 2014;32:1302-1308.

Nemvaleukin alfa is a novel, engineered cytokine



- Preferential activation of high-affinity IL-2R leads to T_{reg} expansion, which may counteract antitumor activity
- 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

IL-2, interleukin-2; IL-2R, IL-2 receptor; NK, natural killer; T_{reg}, regulatory T cell.
Lopes JE, et al. *J Immunother Cancer*. 2020;8(1):e000673.

Potential for nemvaleukin in PROC

- Preclinical antitumor activity of multiple agents, including chemotherapy, CPIs, and TKIs, is enhanced when each is used in combination with nemvaleukin[1-3]
- ARTISTRY-1 (NCT02799095): phase 1/2 trial evaluating nemvaleukin alone and in combination with pembrolizumab in patients with advanced solid tumors, including PROC
- We describe findings from nemvaleukin plus pembrolizumab in patients with PROC enrolled in ARTISTRY-1

CPI, checkpoint inhibitor; TKI, tyrosine kinase inhibitor.

1. Losey HC, et al. *Cancer Res.* 2017;77(13 Suppl):Abstr 591. 2. Lopes JE, et al. *Cancer Res.* 2020;80(16 Suppl):Abstr 2202. 3. Pan Y, et al. *Ann Oncol.* 2021;32(Supp1_5):Abstr 1661P.

ARTISTRY-1 study design and PROC cohort

Monotherapy cohort
Nemvaleukin dose escalation
Dose cohorts: 0.1-10 µg/kg IV

Combination therapy cohort (N=162)[a]
Nemvaleukin + pembrolizumab

- **Objectives:** Characterize safety profile and antitumor activity by ORR[b]
- **Cohorts:** Mixed tumor types based on PD-(L)1 indication and prior treatment received nemvaleukin 3 µg/kg IV; additional tumor-specific cohorts received nemvaleukin 6 µg/kg IV

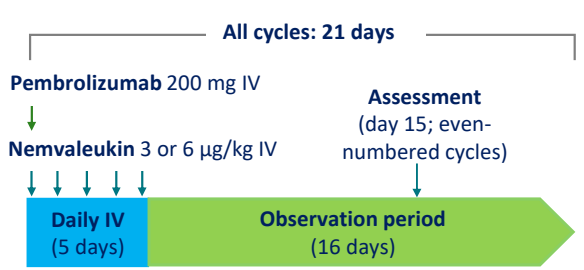
PD-(L)1 unapproved cohort (n=42)

- 9 different tumor types, primarily CRC, PROC, and sarcoma

PROC population (n=16[c])

- Advanced solid tumors, refractory to or intolerant of established therapies known to provide clinical benefit
- Prior therapy with platinum-based regimens
- ECOG PS 0 or 1 with life expectancy ≥3 months
- Adequate hematologic reserve, hepatic function, and renal function

Combination dosing regimen



[a]3 patients received nemvaleukin 1 µg/kg. [b]Assessed by investigator (RECIST v1.1). [c]1 patient had platinum-refractory disease and 1 patient received nemvaleukin 1 µg/kg.
CRC, colorectal cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; ORR, objective response rate; PD-(L)1, programmed death (ligand) 1; RCC, renal cell carcinoma; RECIST, Response Evaluation Criteria In Solid Tumors.

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Patient baseline characteristics and prior regimens

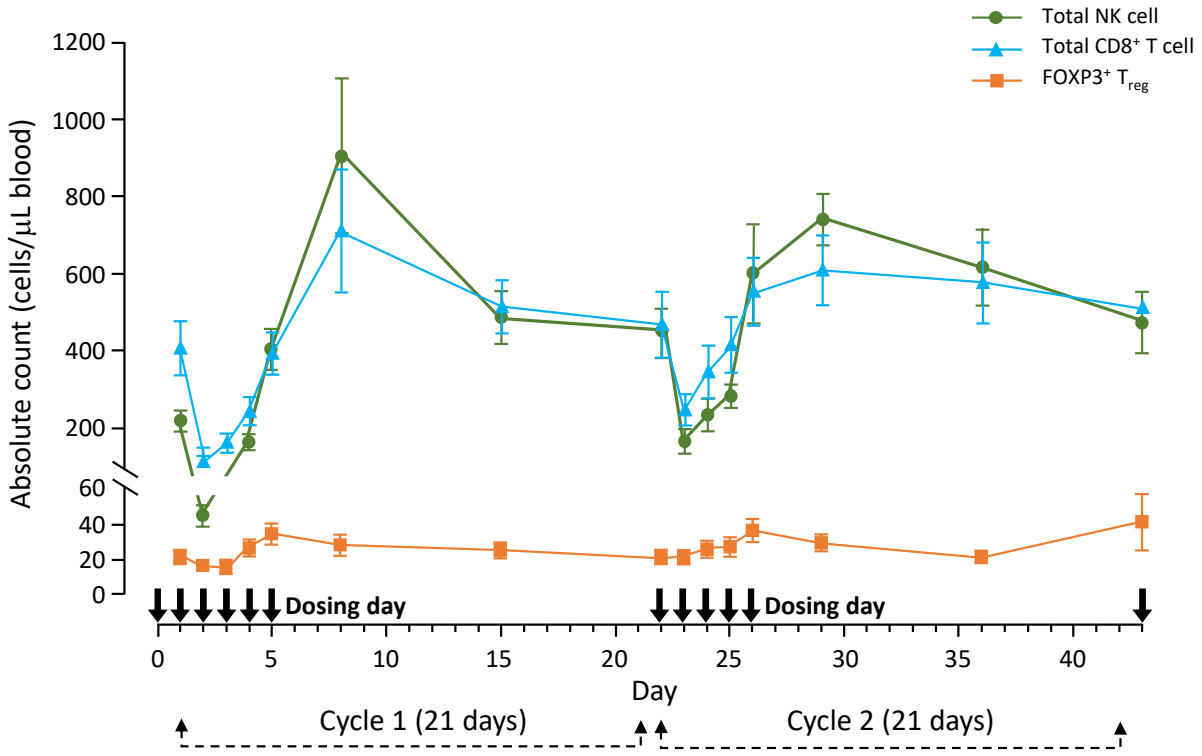
Characteristic	N=15[a]
Age, years, median (range)	63 (48-83)
Race, white, n (%)	11 (73)
ECOG PS, 0 / 1, n (%)	4 (27) / 11 (73)
CA125, U/mL, mean (range)	779 (11-1958)
Histology, HGSOC / Other, n (%)	12 (80) / 3 (20)
PD-L1 status, n (%)	
Positive	2 (13)
Low	2 (13)
Negative	5 (33)
Unknown	6 (40)
Tumor mutational burden, n (%)	
Low	7 (47)
Intermediate	2 (13)
High	0 (0)
Unknown	6 (40)
Microsatellite stable / Unknown, n (%)	11 (73) / 4 (27)
BRCA mutant, n (%)	3 (20)

Prior regimens	N=15[a]
Prior lines of therapy, median (range)	5 (2-6)
Number of prior lines of therapy, n (%)	
<5	7 (46)
≥5	8 (53)
Prior platinum-based therapy, n (%)	15 (100)
Prior bevacizumab, n (%)	9 (60)
Prior PARP inhibitor, n (%)	6 (40)
Prior anti-PD-(L)1 CPI, n (%)	3 (20)
BOR to last line of therapy, n (%)	
CR or PR	3 (20)
SD	4 (27)
PD	8 (53)

[a]Excludes 1 patient who received nemvaleukin 1 µg/kg.
BOR, best overall response; *BRCA*, breast cancer gene; CA125, cancer antigen 125; CR, complete response; HGSOC, high-grade serous ovarian cancer; PARP, poly ADP ribose polymerase; PD, progressive disease; PR, partial response; SD, stable disease.

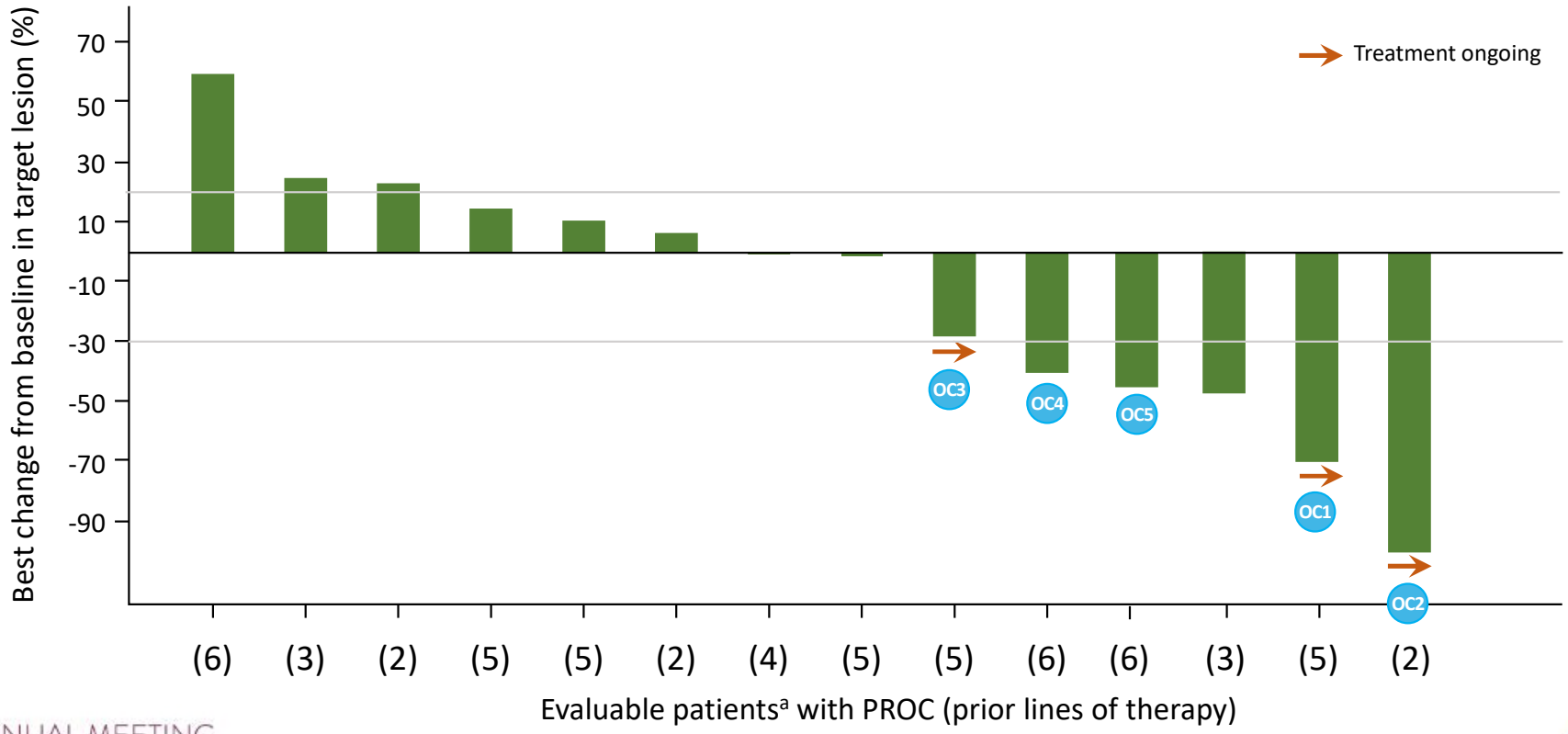
Nemvaleukin + pembrolizumab induced robust expansion of CD8$^+$ T and NK cells, with minimal effect on T_{regs}

- 15 patients with PROC who received nemvaleukin 3 µg/kg IV + pembrolizumab



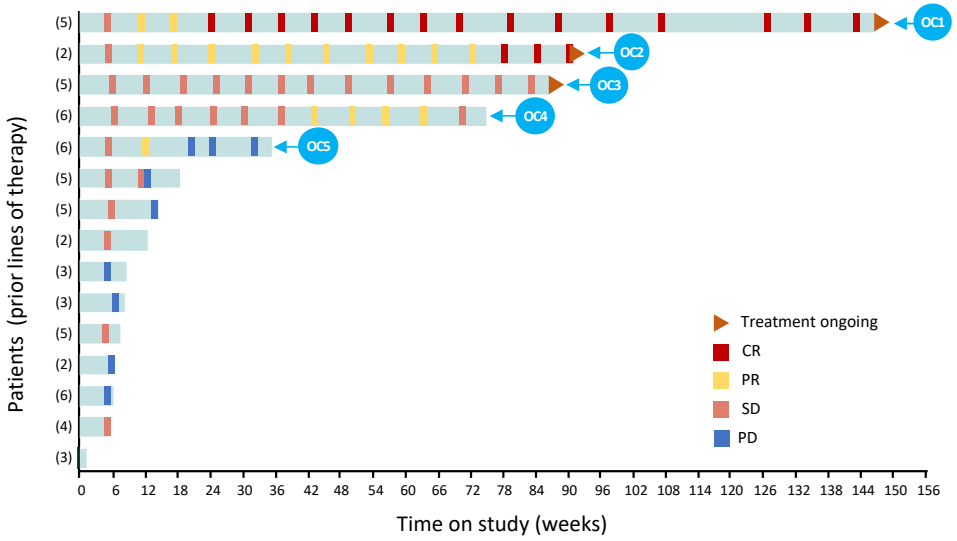
Bars represent standard error.
FOXP3, Forkhead box P3.

Best change from baseline of target lesion sum



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

Antitumor activity of nemvaleukin + pembrolizumab



Summary of patient experience

Patient	Age (years)	Number of prior regimens/ Prior therapies	Best overall response[a]	Maximum change in target lesions (%)	Time on therapy (weeks)
OC1	48	5: CBP/PAC/BEV, CDDP/GEM, CBP/ PLD, PCA, CBP/DOC	CR	↓ 70	146 ▶
OC2	83	2: CBP/PAC/DOC, CBP/DOC/NIR/TAM	CR	↓ 100	90 ▶
OC3	83	5: CBP/PAC, CBP, CBP/PAC/CAP, CBP/PLD/PEG, CBP/PLD	SD	↓ 28	86 ▶
OC4	75	6: CBP/PAC, NIR, PLD/BEV, CBP/GEM, TOP, NIR	PR	↓ 41	75
OC5	60	6: CBP/PAC, CBP/PLD, CBP/BEV, PAC/BEV, BEV, PLD	uPR	↓ 45	36

▶ Treatment ongoing.

- 5 patients with PROC had clinically meaningful benefit, 4 of whom were on treatment >1 year
  - 4 objective responses: 2 CRs, 2 PRs (1 unconfirmed); 1 SD for >1.5 years
  - 3 of these patients remain on treatment
- ORR was 28.6% and DCR was 71.4% in 14 evaluable patients[b] who received nemvaleukin 3 µg/kg IV + pembrolizumab

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[a]Assessed by investigator. [b]Patients who received nemvaleukin 3 µg/kg IV + pembrolizumab and had ≥1 post-baseline scan. BEV, bevacizumab; CAP, capecitabine; CBP, carboplatin; CDDP, cisplatin; DCR, disease control rate (CR+PR+SD); DOC, docetaxel; GEM, gemcitabine; NIR, niraparib; PAC, paclitaxel; PCA, paclitaxel albumin; PEG, pegfilgrastim; PLD, pegylated liposomal doxorubicin hydrochloride; TAM, tamoxifen; TOP, topotecan; uPR, unconfirmed PR. Data cutoff October 29, 2021.

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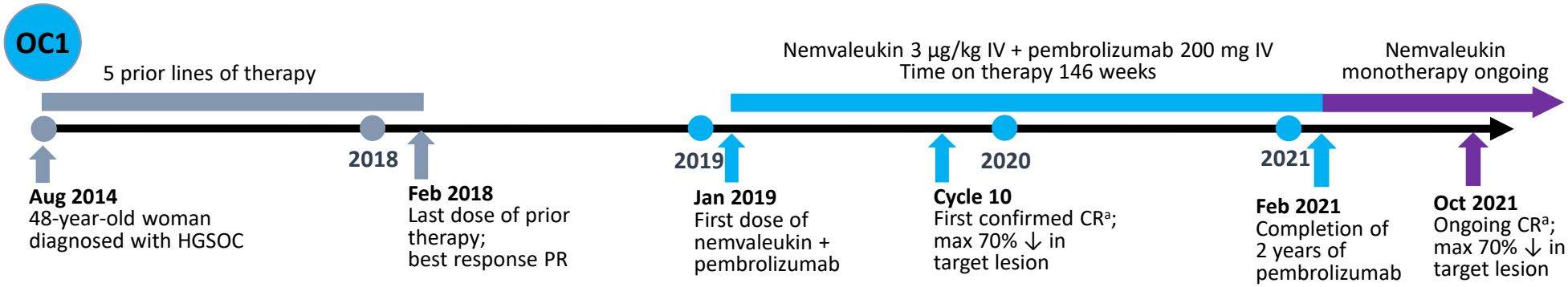
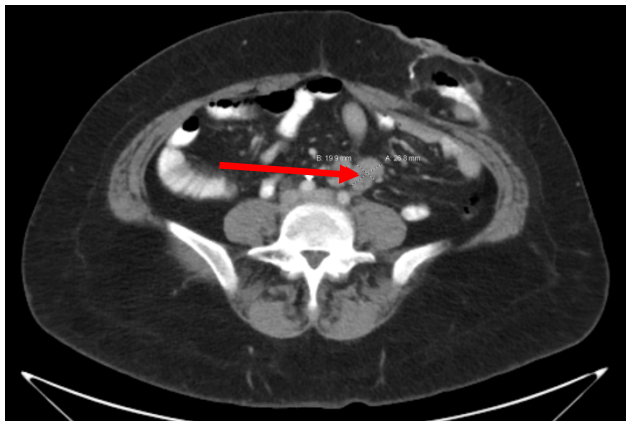
Complete response in patient OC1

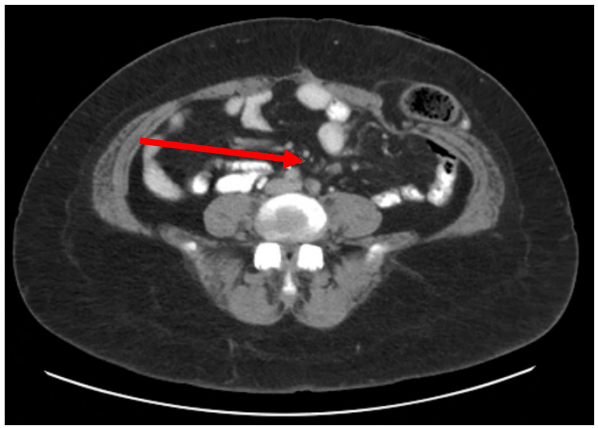


- The combination therapy was well tolerated

Lymph node



Baseline
27DEC2018



Cycle 50[b]
13DEC21

[a]Response per RECIST v1.1. [b]Beyond data cutoff date.

Complete response in patient OC2

OC2

2 prior lines of therapy

Nemvaleukin 3 µg/kg IV + pembrolizumab 200 mg IV
Time on therapy 90 weeks; treatment ongoing

2018 | 2019 | 2020 | 2021

Oct 2008
83-year-old woman diagnosed with HGSOC

Dec 2018
Last dose of prior therapy;
best response CR

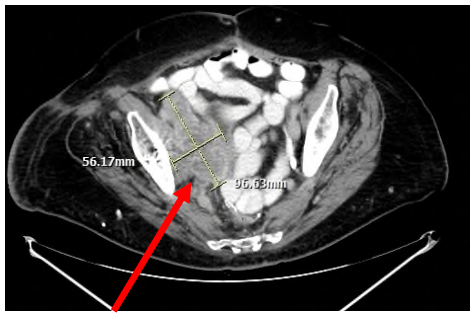
Feb 2020
First dose of nemvaleukin + pembrolizumab

Apr 2020
Cycle 4
First PR[a];
55% ↓ in target lesion

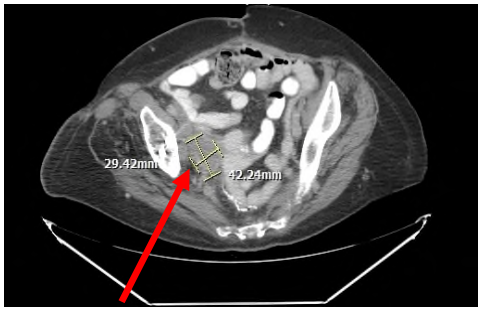
Aug 2021
Cycle 24 First CR[a]
Oct 2021: Ongoing CR[a]; max 100% ↓ in target lesion; continuing therapy

- The combination therapy was well tolerated

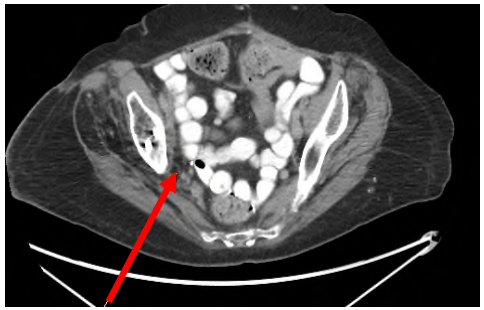
Right hemipelvic lesion



Baseline
29JAN2020



Cycle 4
21APR2020
PR



Cycle 24
03AUG2021
CR

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[a]Response per RECIST v1.1.

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Safety of nemvaleukin + pembrolizumab

Event, n (%)	N=162
Any AE	156 (96.3)
Serious AEs	66 (40.7)
Nemvaleukin-related AEs	146 (90.1)
Grade 1 or 2	144 (88.9)
Grade 3 or 4	76 (46.9)
AEs leading to discontinuation	16 (9.9)
Nemvaleukin-related AEs leading to discontinuation	6 (3.7)
Nemvaleukin-related AEs leading to death	1 (1)

Combination treatment cohort[a] (N=162)

- Most frequent nemvaleukin-related Grade 3-4 AEs: anemia (9.9%), neutropenia (9.3%), and decreased neutrophil count (9.3%)
- 1 nemvaleukin-related AE leading to death (inanition) in a heavily pretreated patient with pancreatic cancer

[a]Nemvaleukin 3 or 6 µg/kg IV + pembrolizumab (n=159); nemvaleukin 1 µg/kg IV + pembrolizumab (n=3).
AE, adverse event.

Conclusions

- Nemvaleukin + pembrolizumab combination showed evidence of tumor response and disease control in patients with heavily pretreated PROC
  - Includes 2 durable complete responses among 14 evaluable patients with PROC; both still on treatment after ~2 years
- Combination therapy was generally well tolerated
  - Safety profile in patients with PROC was consistent with that in the overall safety population
- Antitumor activity also observed in PROC cohort of phase 1/2 ARTISTRY-2 trial of subcutaneous nemvaleukin + pembrolizumab[1]
- US FDA granted Fast Track Designation to nemvaleukin + pembrolizumab for treatment of PROC
- Phase 3 ARTISTRY-7 trial in patients with PROC will further evaluate nemvaleukin + pembrolizumab; trial is ongoing and recruiting (**see Herzog et al. Abstract 119031 at this congress**[2])

1. Hamid O, et al. *J Clin Oncol*. 2021;39(Suppl 15):Abstr 2552. 2. Herzog TJ, et al. 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. Abstract ID 11903.
ARTISTRY-7: NCT05092360; ARTISTRY-2: NCT03861793.

Acknowledgments

- The authors would like to thank all of the patients who are participating in this trial and their families
- Many thanks to all of the investigators and site personnel for their participation in this study. Special gratitude to the following individuals for help obtaining radiology, pathology, and genetic profiling reports: Jana Adams, Rachael Gorney, Christine Gerdes, Taylor Grant, Phoebe Hannon, Ashley Jackson, Stephanie Stamatis, and Nithin Thummala
- The trial is sponsored by Alkermes, Inc.
- Medical writing and editorial support was provided by Parexel and funded by Alkermes, Inc.