2022 ASCO® ANNUAL MEETING

Abstract # 2500

Nemvaleukin Alfa Monotherapy and in Combination With Pembrolizumab in Patients With Advanced Solid Tumors: ARTISTRY-1

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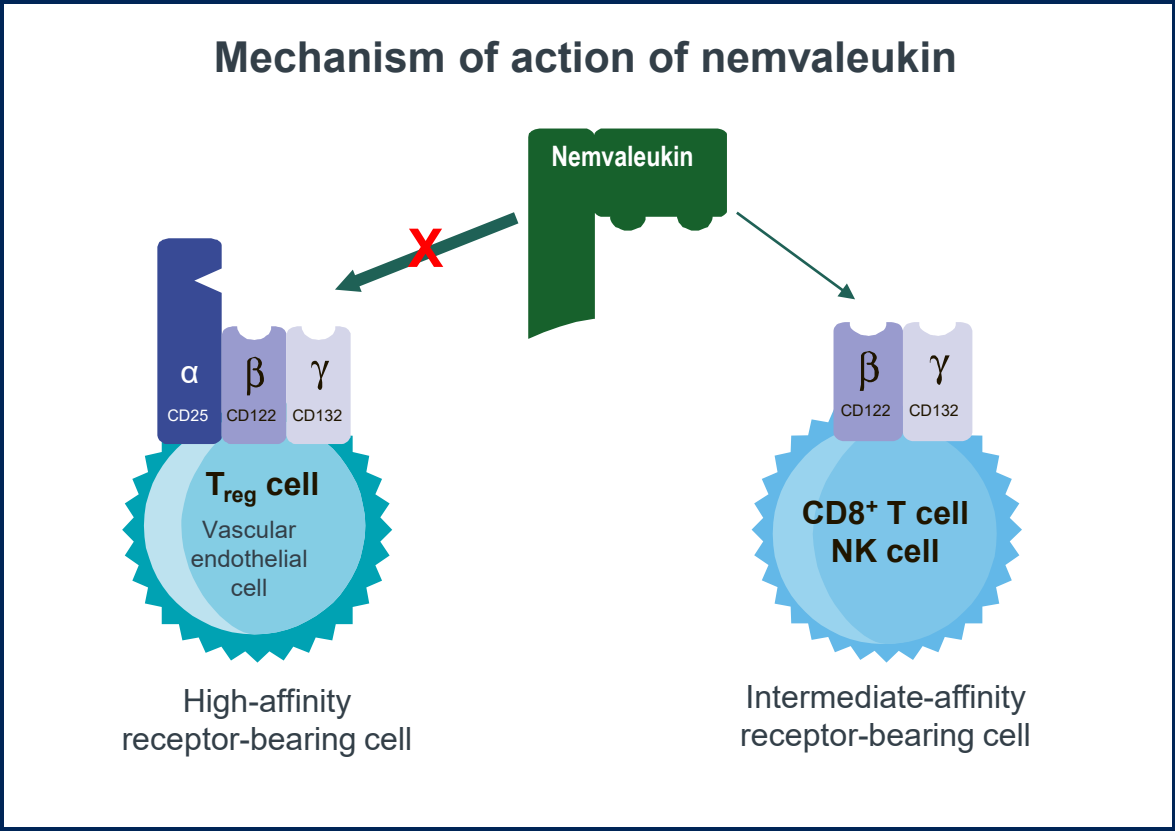
Nemvaleukin: novel engineered cytokine designed to leverage antitumor effects of high-dose IL-2

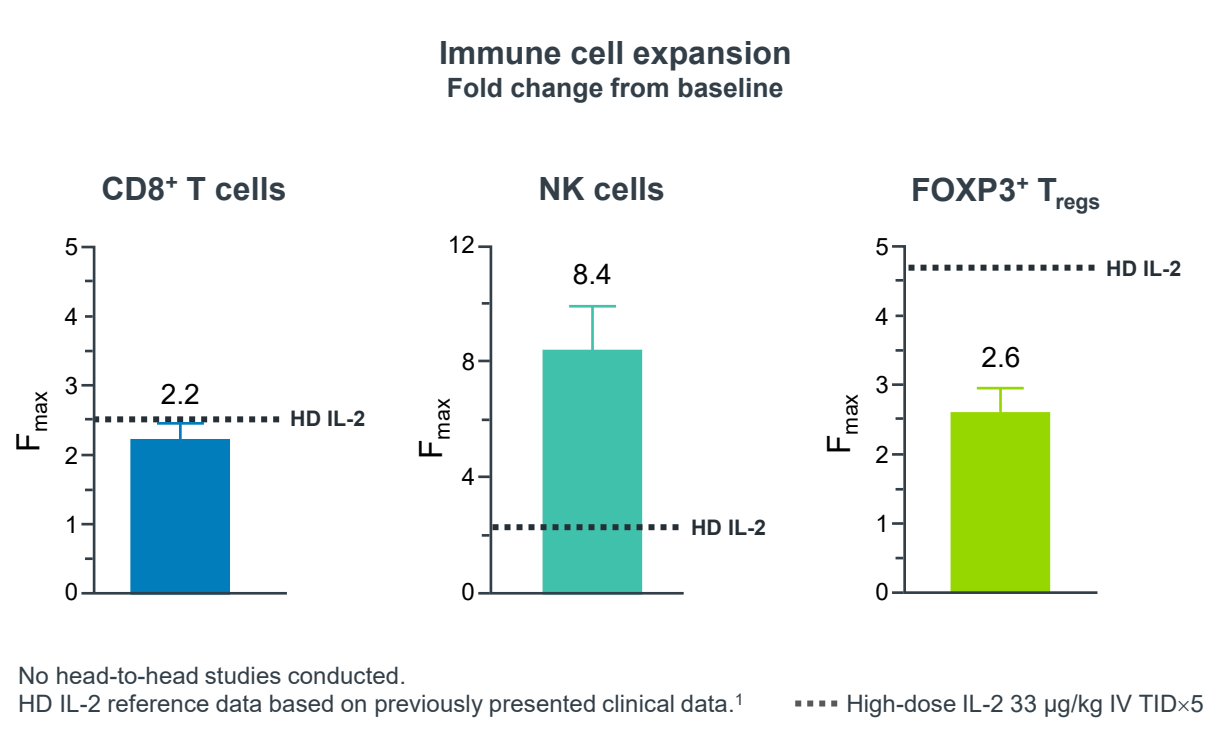


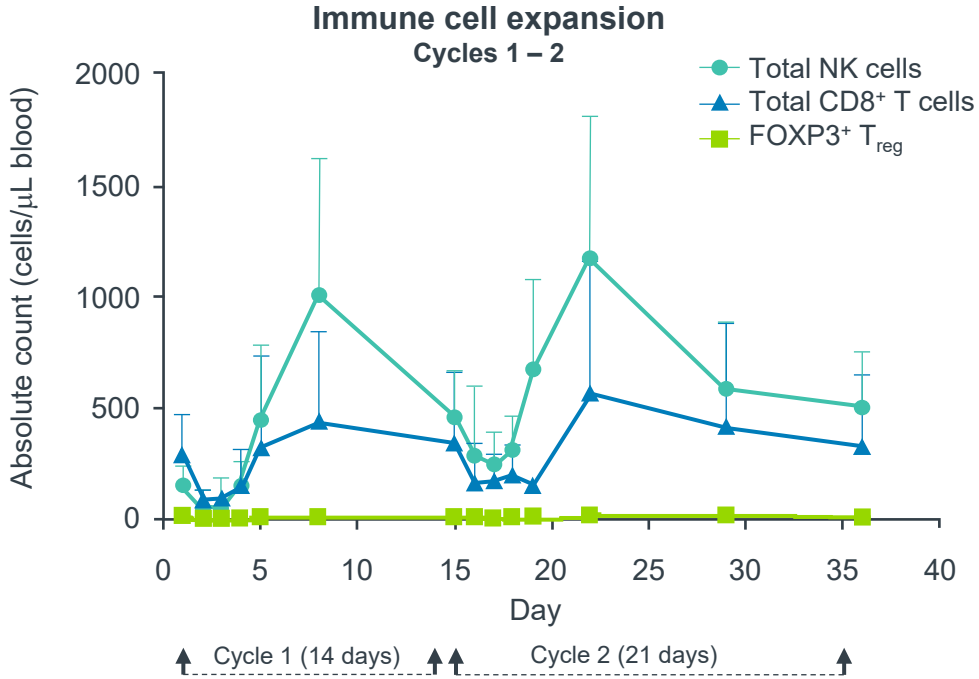
- Intrinsically active, stable fusion protein; does not degrade into native IL-2
- Selectively binds to the intermediate-affinity IL-2R
- Designed to mitigate toxicities associated with high-dose IL-2

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

Nemvaleukin: novel engineered cytokine designed to leverage antitumor effects of high-dose IL-2

Clinical pharmacodynamic effects





- Design hypothesis established by PD effect
- Unlike high-dose IL-2, minimal non–dose-dependent effect on T_{regs}

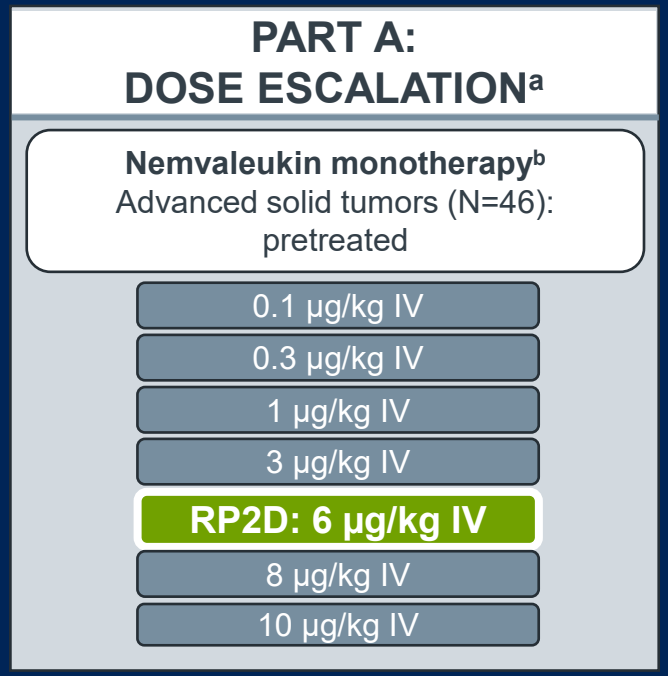
Nemvaleukin data are from the 6 µg/kg cohort in Part A of the study. For fold change plots, data are mean + SE (N=10). For time course plot, data are mean + SD (N=12).

1. Bhatt et al. Poster P123 presented at SITC 2018.

F_{max}, maximum fold change; HD, high-dose; IL-2, interleukin-2; IV, intravenous; NK, natural killer; PD, pharmacodynamic; SD, standard deviation; SE, standard error; TID, 3 times daily; T_{reg}, regulatory T cell.

ARTISTRY-1: first-in-human study of IV nemvaleukin

Global, multicenter, open-label phase 1/2 study



All data in this presentation are as of Oct 29, 2021, unless otherwise noted

NCT02799095

[a]Patients from Parts A and B could roll over to Part C upon progression or stable disease (after ≥4 cycles) on monotherapy. [b]Nemvaleukin daily for 5 days, then off treatment for 9 days (cycle 1) or 16 days (cycle 2+). [c]ORR assessed by investigator (RECIST v1.1). [d]Nemvaleukin 3 µg/kg/d in C1-C4, 6 µg/kg/d in C5-C7. [d]PD-(L)1 approved/unapproved indication based on US FDA prescribing information and may have changed over time.
C1-7, Cohort 1-7; CPI, checkpoint inhibitor; HNSCC, head and neck squamous cell carcinoma; IV, intravenous; NSCLC, non–small cell lung cancer; ORR, overall response rate; PD-(L)1, programmed death (ligand) 1; RCC, renal cell carcinoma; RP2D, recommended phase 2 dose.

ARTISTRY-1: first-in-human study of IV nemvaleukin

Global, multicenter, open-label phase 1/2 study

PART A: DOSE ESCALATION[a]

Nemvaleukin monotherapy[b]
Advanced solid tumors (N=46): pretreated

- 0.1 µg/kg IV
- 0.3 µg/kg IV
- 1 µg/kg IV
- 3 µg/kg IV
- **RP2D: 6 µg/kg IV**
- 8 µg/kg IV
- 10 µg/kg IV

All data in this presentation are as of Oct 29, 2021, unless otherwise noted

DOSE EXPANSION

PART B: MONOTHERAPY[a]

RP2D: Nemvaleukin 6 µg/kg IV[b]

- Advanced melanoma (n=47): CPI pretreated
- Advanced RCC (n=27): CPI naive or pretreated

Objectives: safety and antitumor activity[c]

NCT02799095

[a]Patients from Parts A and B could roll over to Part C upon progression or stable disease (after ≥4 cycles) on monotherapy. [b]Nemvaleukin daily for 5 days, then off treatment for 9 days (cycle 1) or 16 days (cycle 2+). [c]ORR assessed by investigator (RECIST v1.1). [d]Nemvaleukin 3 µg/kg/d in C1-C4, 6 µg/kg/d in C5-C7. [d]PD-(L)1 approved/unapproved indication based on US FDA prescribing information and may have changed over time.
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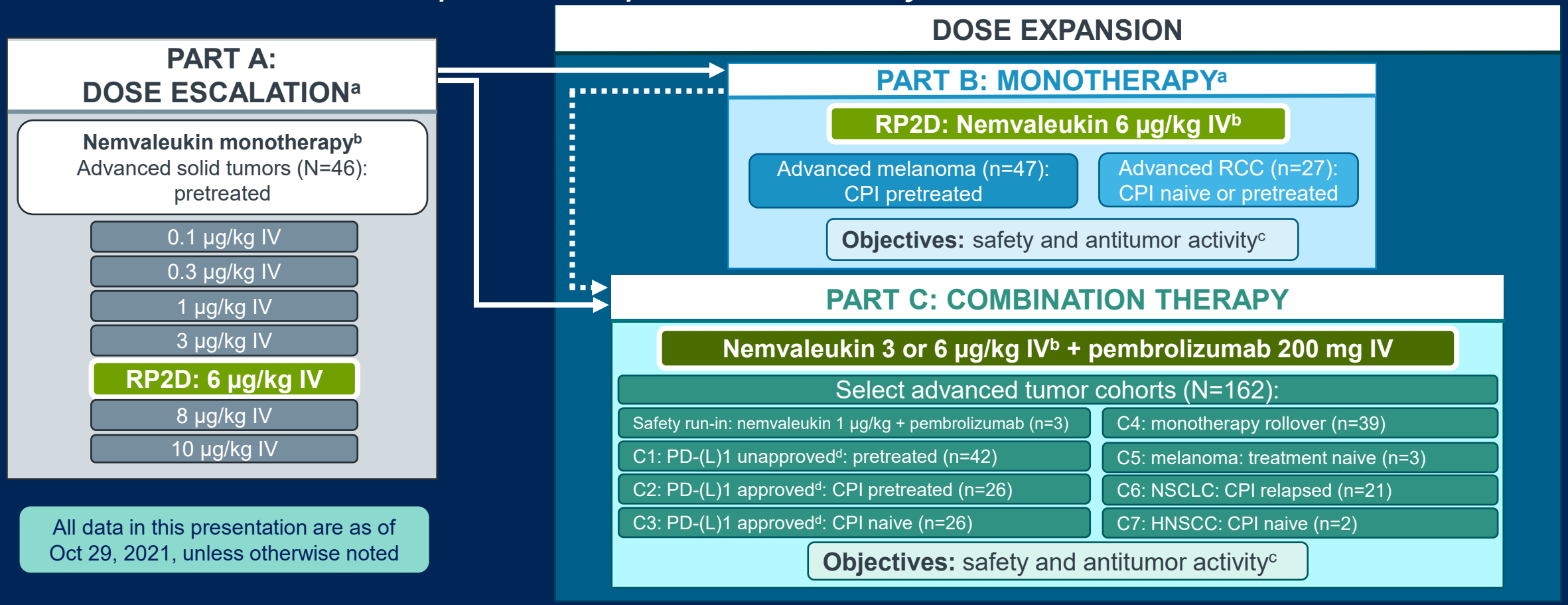
ARTISTRY-1: first-in-human study of IV nemvaleukin

Global, multicenter, open-label phase 1/2 study



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[a]Patients from Parts A and B could roll over to Part C upon progression or stable disease (after ≥4 cycles) on monotherapy. [b]Nemvaleukin daily for 5 days, then off treatment for 9 days (cycle 1) or 16 days (cycle 2+). [c]ORR assessed by investigator (RECIST v1.1). [d]Nemvaleukin 3 µg/kg/d in C1-C4, 6 µg/kg/d in C5-C7. [d]PD-(L)1 approved/unapproved indication based on US FDA prescribing information and may have changed over time.
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RP2D established as 6 µg/kg based on PK, PD, & safety

Monotherapy dose escalation (Part A)

Baseline characteristics	Overall (N=46)
Median age, years	60
ECOG PS, n (%)	
0	18 (39)
1	28 (61)
Median prior lines of therapy (range)	3 (1-8)
Primary origin of tumor type, n (%)	
Melanoma	10 (22)
RCC	6 (13)
Ovarian	2 (4)
Other	28 (61)

- Nemvaleukin generally well tolerated across doses tested
- Dose-dependent increases in nemvaleukin systemic exposure
  - At 6 µg/kg IV, mean half-life after first dose was ~5 hours
- RP2D dose: 6 µg/kg IV on days 1-5 of a 21-day cycle
- MTD not reached
  - Highest dose tested (10 µg/kg)

ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; MTD, maximum tolerated dose; PD, pharmacodynamics; PK, pharmacokinetics; RCC, renal cell carcinoma; RP2D, recommended phase 2 dose.

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Ulka Vaishampayan

Baseline demographics and prior therapies

Dose expansion: monotherapy and combination therapy

Monotherapy (Part B)		
	Melanoma (n=47)	RCC (n=27)
Median age, years	66	69
ECOG PS, n (%)		
0	23 (49)	7 (26)
1	24 (51)	20 (74)
Median prior lines of therapy (range)	3 (1-8)	2 (1-8)
Histology, n (%)		
Cutaneous	30 (64)	NA
Mucosal	7 (15)	NA
Uveal	6 (13)	NA
Acral	4 (9)	NA
CPI pretreated, n (%)		
Yes	45 (96)	15 (56)
No	2 (4)	12 (44)

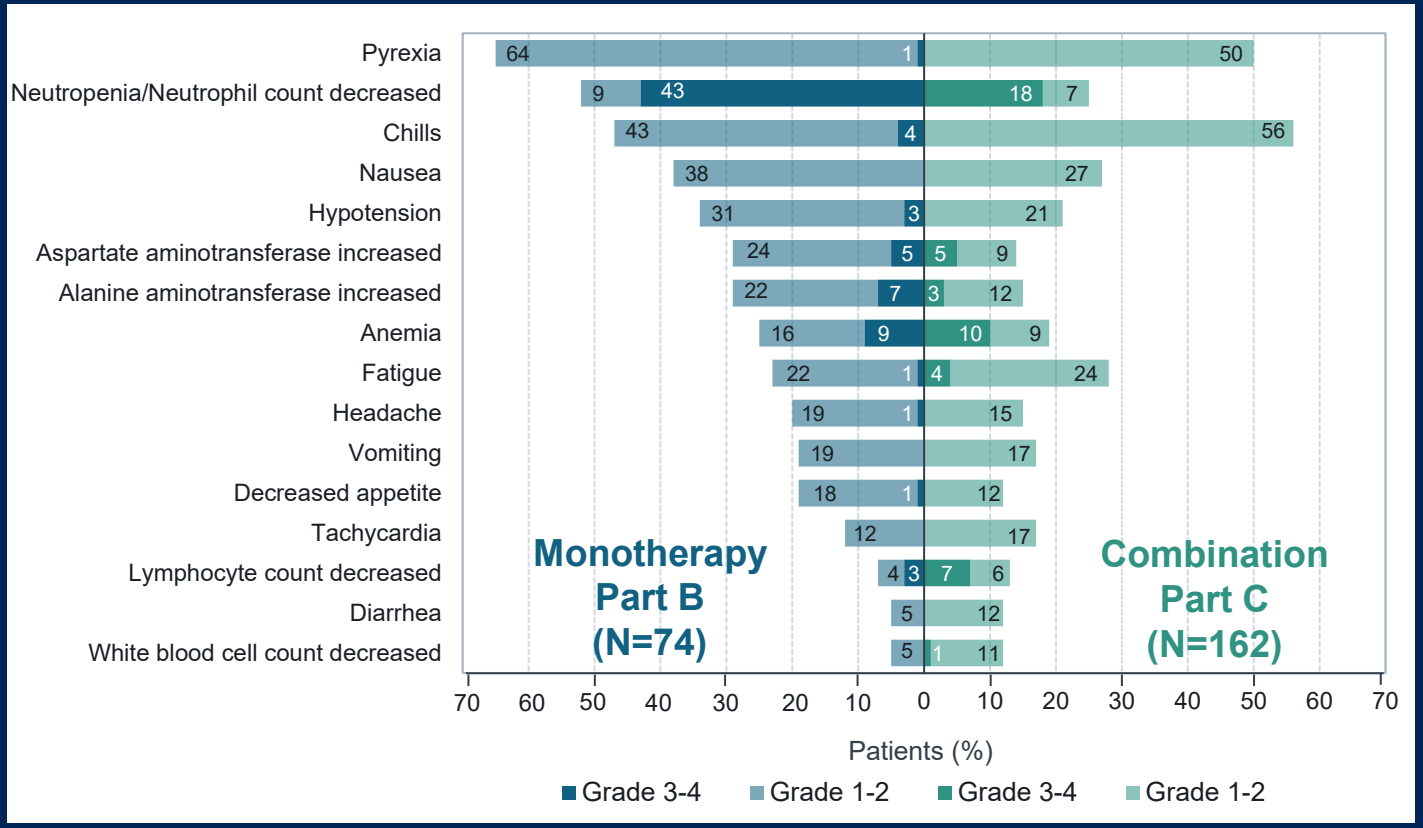
Combination with pembrolizumab (Part C)	
	Overall (N=162)
Median age, years	62
ECOG PS, n (%)	
0	50 (31)
1	112 (69)
Median prior lines of therapy (range)	3 (1-9)
Most common tumor types, n (%)	
NSCLC	29 (18)
Melanoma	28 (17)
Ovarian	17 (11)
Colorectal	13 (8)
SCLC	8 (5)

CPI, checkpoint inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; NA, not applicable; NSCLC, non–small cell lung cancer; RCC, renal cell carcinoma; SCLC, small-cell lung cancer.

Overall safety summary

Dose expansion: monotherapy and combination therapy

Summary of most frequent TRAEs (≥10% in either cohort)

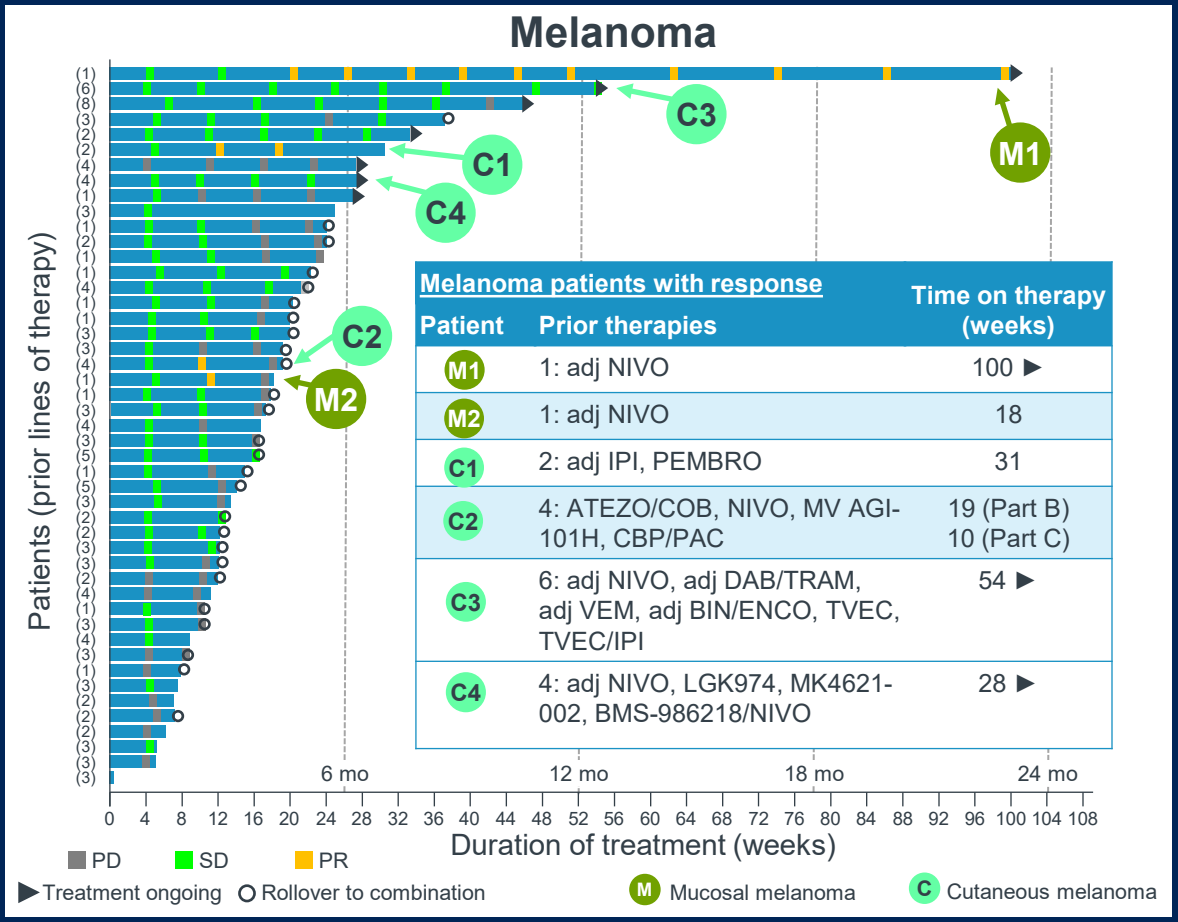


- AE profile consistent with nemvaleukin mechanism of action
- Monotherapy safety profile is similar to combination, with no additive toxicity
- Most frequently observed grade 3-4 TRAE: neutropenia[a]
  - Median duration 4 days; not associated with risk of serious infections or febrile neutropenia
- TRAEs leading to discontinuation: 3% (monotherapy), 4% (combination)
- No event of capillary leak syndrome reported to date

Part C includes patients who received nemvaleukin at 1, 3, or 6 µg/kg IV in combination with pembrolizumab 200 mg IV.
[a]Includes neutropenia and decreased neutrophil count.
AE, adverse event; IV, intravenous; TRAE, treatment-related AE.

Melanoma: duration of treatment and summary of responses

Dose expansion (Part B, monotherapy)



Melanoma patients with response

Patient	Prior therapies	Time on therapy (weeks)
M1	1: adj NIVO	100 ▶
M2	1: adj NIVO	18
C1	2: adj IPI, PEMBRO	31
C2	4: ATEZO/COB, NIVO, MV AGI-101H, CBP/PAC	19 (Part B) 10 (Part C)
C3	6: adj NIVO, adj DAB/TRAM, adj VEM, adj BIN/ENCO, TVEC, TVEC/IPI	54 ▶
C4	4: adj NIVO, LGK974, MK4621-002, BMS-986218/NIVO	28 ▶

	All[a,b] (N=46)	Mucosal (n=6)
Best overall response, n (%)		
CR	0	0
PR	6 (13.0)[c]	2 (33.3)[d]
SD	31 (67.4)	2 (33.3)
PD	9 (19.6)	2 (33.3)
ORR, n (%) [95% CI]	6 (13.0) [4.9-26.3]	2 (33.3) [4.3-77.8]
DCR, n (%) [95% CI]	37 (80.4) [66.1-90.6]	4 (66.7) [22.3-95.7]
Median DOR,[e] weeks (range)	8.1 (6.1-79.0)	NA (6.1-79.0)

[a]1 patient did not meet tumor-evaluable criteria. [b]Patients with mucosal, cutaneous, uveal, acral included in All. [c]Includes 3 confirmed PRs (1 occurred after data cutoff date), 2 unconfirmed PRs, and 1 PR awaiting confirmation (occurred after data cutoff date). [d]1 confirmed PR. [e]DOR for Part B only and does not include patients who rolled over to Part C; some patients may still be on treatment.

All responders had been on prior CPI therapy and progressed

FDA ODD and FTD designations granted in mucosal melanoma

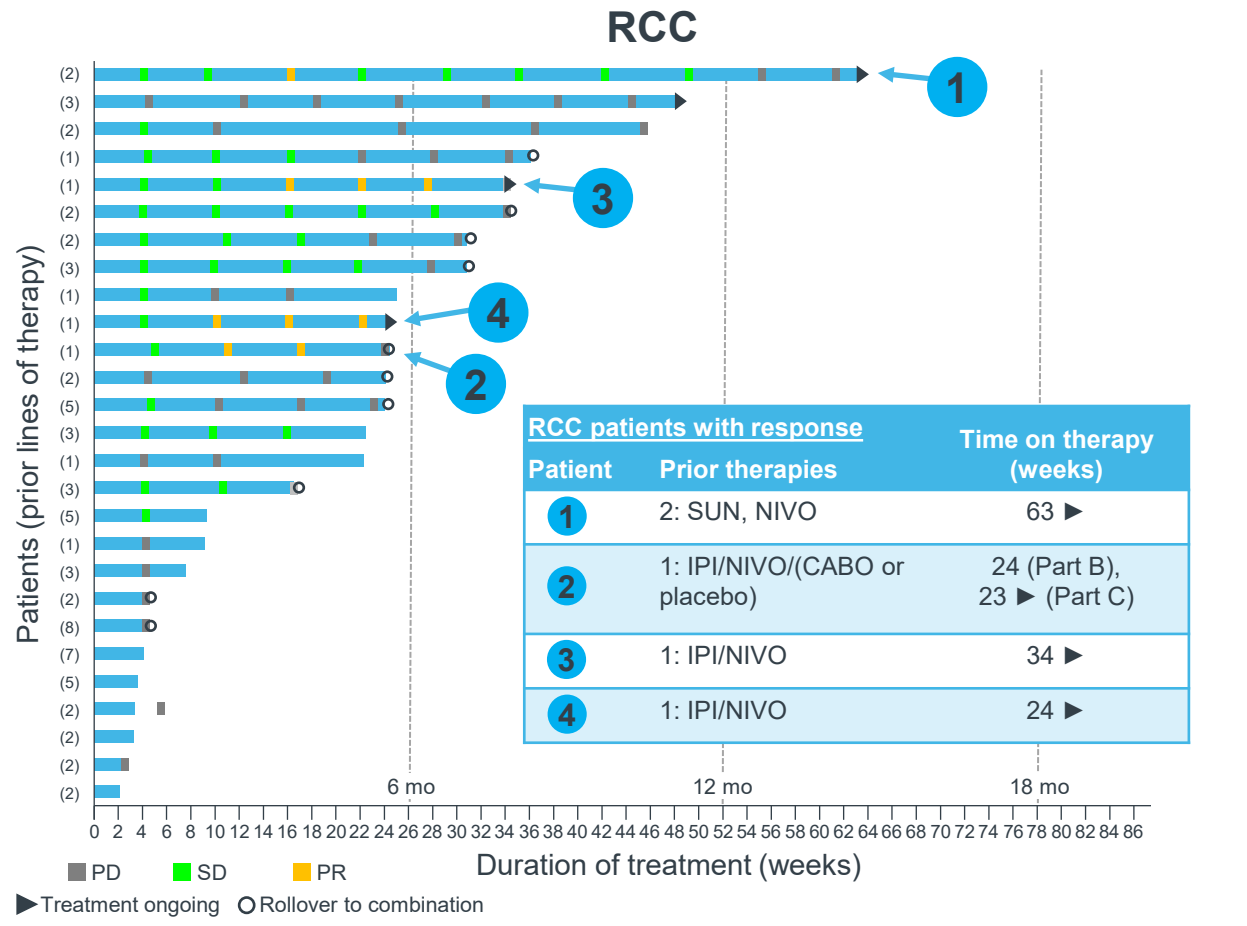
Data supported design of ARTISTRY-6 study
(see Weber et al. poster # TPS9609 at this congress)

Responses per RECIST v1.1.

adj, adjuvant; ATEZO, atezolizumab; BIN, binimetinib; CBP, carboplatin; CI, confidence interval; COB, cobimetinib; CPI, checkpoint inhibitor; CR, complete response; DAB, dabrafenib; DCR, disease control rate (CR+PR+SD); DOR, duration of response; ENCO, encorafenib; FDA, US Food and Drug Administration; FTD, Fast Track designation; IPI, ipilimumab; MV, melanoma vaccine; NA, not applicable; NIVO, nivolumab; ODD, Orphan Drug designation; ORR, overall response rate; PAC, paclitaxel; PD, progressive disease; PEMBRO, pembrolizumab; PR, partial response; SD, stable disease; TRAM, trametinib; TVEC, talimogene laherparepvec; VEM; vemurafenib.

RCC: duration of treatment and summary of responses

Dose expansion (Part B, monotherapy)



	RCC (n=22)[a]
Best overall response, n (%)	
CR	0
PR	4 (18.2)[b]
SD	10 (45.5)
PD	8 (36.4)
ORR, n (%) [95% CI]	4 (18.2) [5.2-40.3]
DCR, n (%) [95% CI]	14 (63.6) [40.7-82.8]
Median DOR,[c] weeks (range)	15.6 (12.3-39.0)

[a]5 patients did not meet tumor-evaluable criteria [b]Includes 3 confirmed PRs and 1 unconfirmed PR. [c]DOR is for Part B only and does not include rollover to Part C; some patients may still be on treatment.

Clinically meaningful responses observed

All responders had been on prior CPI therapy and progressed

Responses per RECIST v1.1.

CABO, cabozantinib; CPI, checkpoint inhibitor; CR, complete response; DCR, disease control rate (CR+PR+SD); DOR, duration of response; IPI, ipilimumab; mo, months; NIVO, nivolumab; ORR, overall response rate (CR+PR); PD, progressive disease; PR, partial response; RCC, renal cell carcinoma; SD, stable disease; SUN, sunitinib.

Best response to treatment: ORR, DCR, DOR

Combination therapy (Part C)

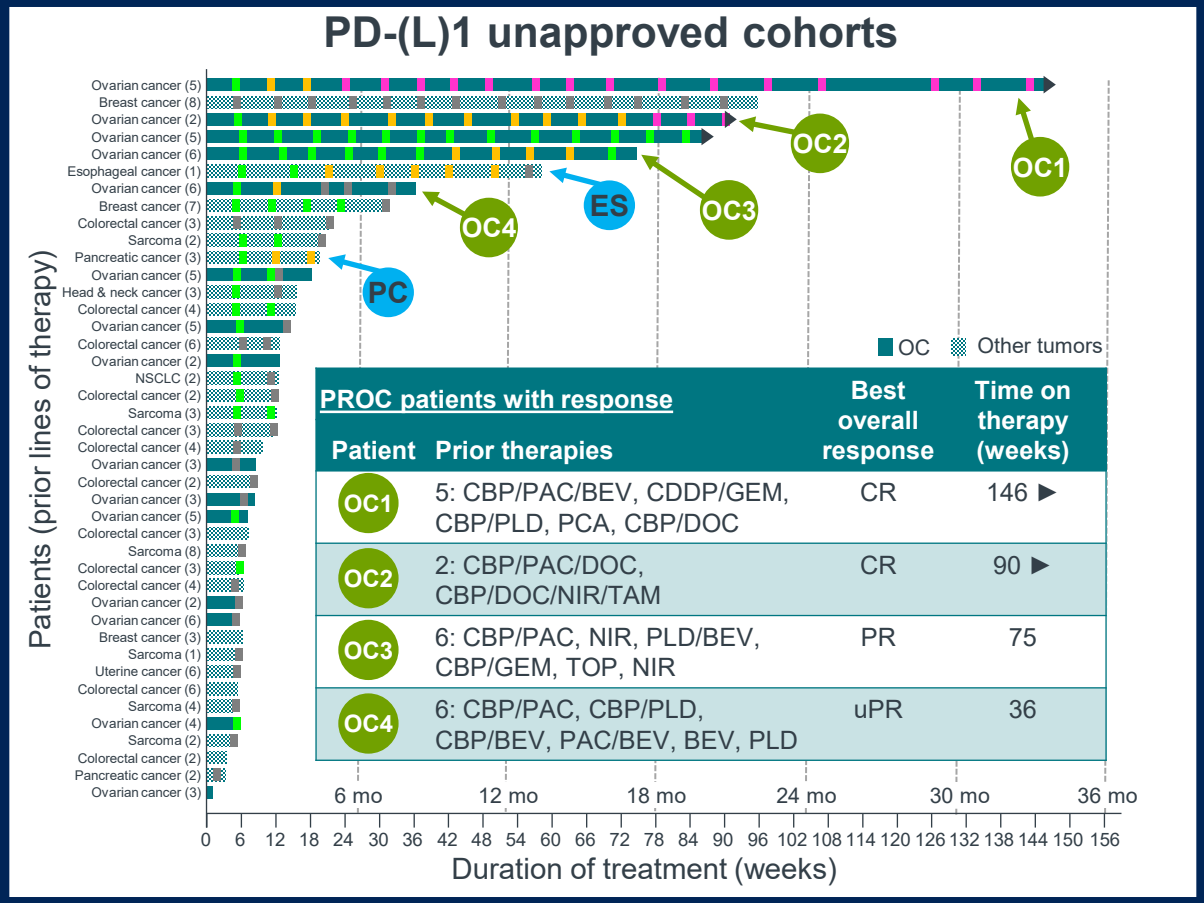
	Overall[a] Cohorts: C1-C7 (N=137)	PD-(L)1 unapproved Cohort: C1 (n=36)	PD-(L)1 approved	
			PD-(L)1 pretreated Cohort: C2 (n=22)	PD-(L)1 naive Cohort: C3 (n=21)
Best overall response,[b] n (%)				
CR	4 (2.9)	2 (5.6)	0	1 (4.8)
PR	18 (13.1)	4 (11.1)	1 (4.5)	6 (28.6)
SD	60 (43.8)	14 (38.9)	10 (45.5)	7 (33.3)
PD	55 (40.1)	16 (44.4)	11 (50.0)	7 (33.3)
ORR, n (%) 95% CI	22 (16.1) 10.3-23.3	6 (16.7) 6.4-32.8	1 (4.5) 0.1-22.8	7 (33.3) 14.6-57.0
DCR, n (%) 95% CI	82 (59.9) 51.1-68.1	20 (55.6) 38.1-72.1	11 (50.0) 28.2-71.8	14 (66.7) 43.0-85.4
Median DOR, weeks Range	23.2 0.1-132.1	27.6 8.3-79.1	NE	26.1 6.9-63.1

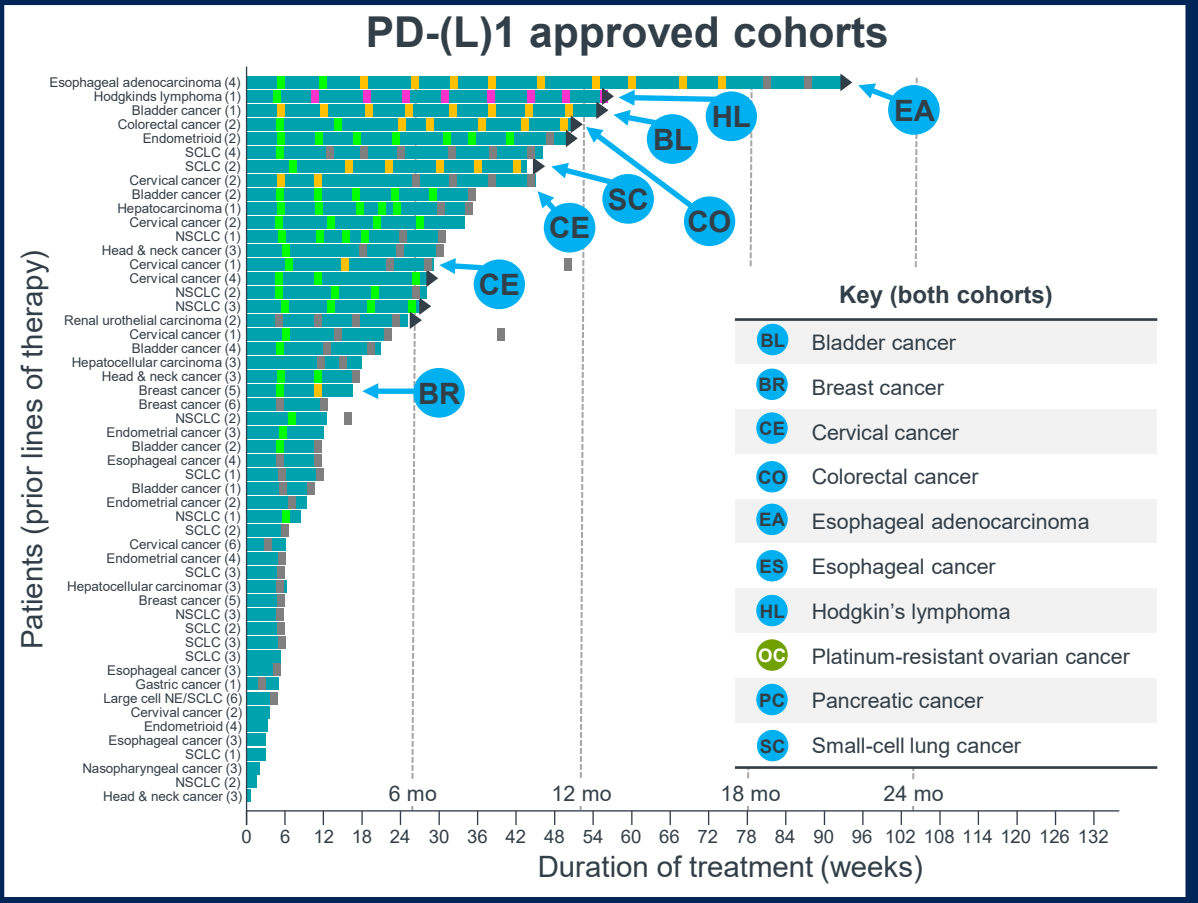
- Antitumor activity observed in various tumor types
  - PROC (n=14): ORR 28.6%; DCR 71.4%; 2 CRs and 2 PRs (1 unconfirmed); median DOR 53.4 weeks
- 43 total patients remain on therapy across the study

[a]The overall column includes patients from all 7 cohorts included in Part C. [b]Responses include confirmed and unconfirmed responses (per RECIST v1.1); percentages are based on patients in the evaluable population.
CR, complete response; DCR, disease control rate (CR+PR+SD); DOR, duration of response; NE, not evaluable; ORR, overall response rate (CR+PR); PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PR, partial response; PROC, platinum-resistant ovarian cancer; SD, stable disease.

Duration of treatment and summary of responses

Combination therapy (Part C)





PD-(L)1 approved/unapproved indication based on US FDA prescribing information and may have changed over time. Responses per RECIST v1.1.

BEV, bevacizumab; CBP, carboplatin; CDDP, cisplatin; CR, complete response; DOC, docetaxel; FDA, Food and Drug Administration; GEM, gemcitabine; mo, month; NIR, niraparib; NSCLC, non–small cell lung cancer; PAC, paclitaxel; PCA, paclitaxel albumin; PD, progressive disease; PD-(L)1, programmed death (ligand) 1; PLD, pegylated liposomal doxorubicin hydrochloride; PR, partial response; PROC, platinum-resistant OC; SCLC, small-cell lung cancer; SD, stable disease; TAM, tamoxifen; TOP, topotecan; uPR, unconfirmed PR.

PD SD PR CR

▶ Treatment ongoing

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Ulka Vaishampayan

Complete response in patient with platinum-resistant ovarian cancer

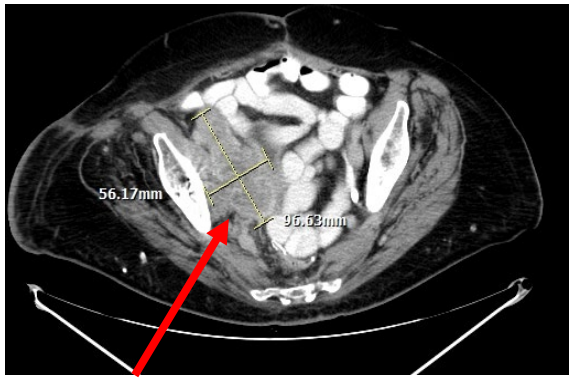
Combination therapy (Part C)

OC2 **83-year-old woman**

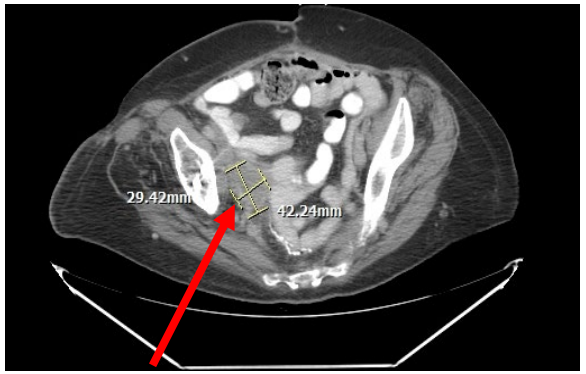
- Diagnosed in 2008 with high-grade serous ovarian cancer
- 2 prior lines of therapy

Nemvaleukin + pembrolizumab
Time on therapy 90 weeks; treatment ongoing

Right hemipelvic lesion

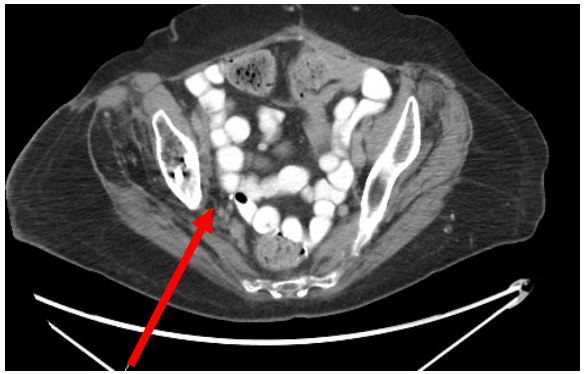


Jan 29, 2020
Baseline



Apr 21, 2020
Cycle 4

PRa 55% ↓ in target lesion



Aug 03, 2021
Cycle 24

CRa Max 100% ↓ in target lesion

[a]Response per RECIST v1.1.

CR, complete response; PR, partial response.

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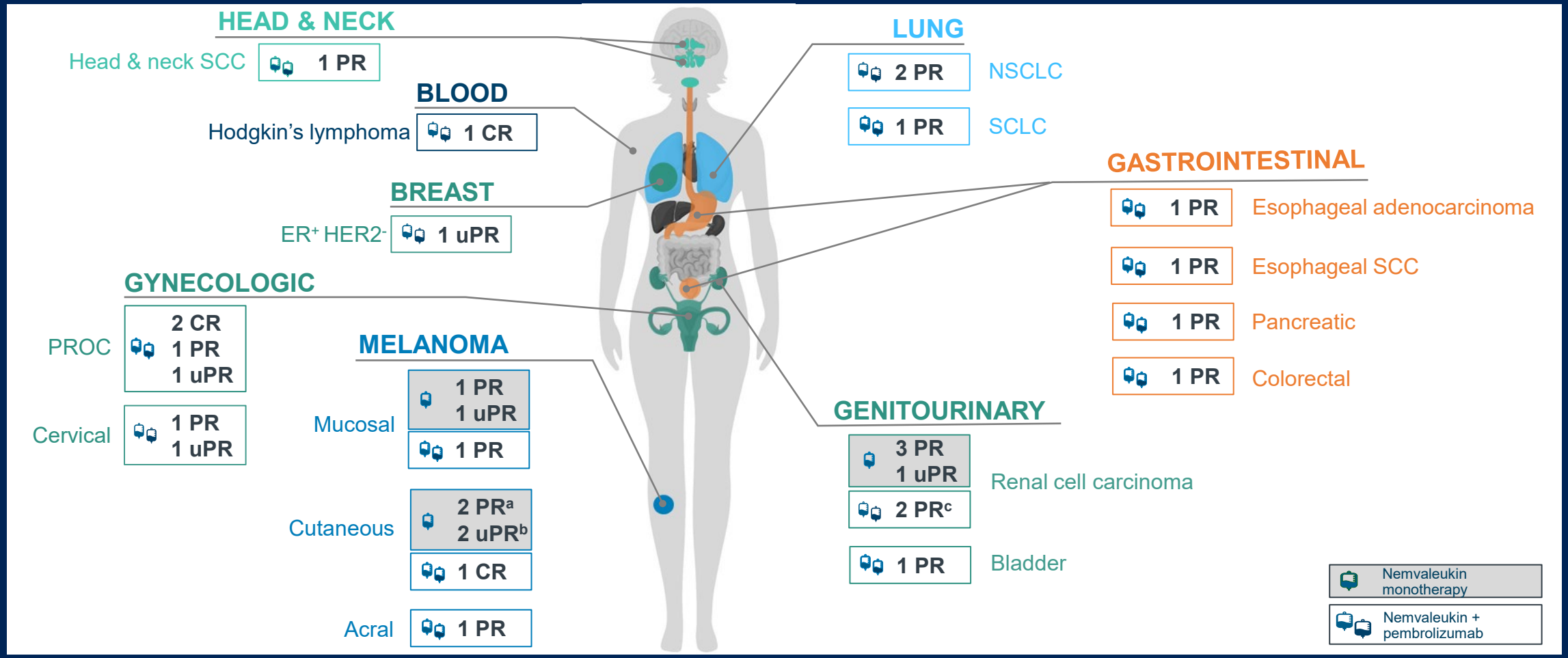
Summary of individual responses

Dose expansion (Part B) and combination therapy (Part C)



[a]1 PR occurred after the data cutoff date. [b]Includes 1 PR awaiting confirmation (occurred after the data cutoff date). [c]Includes 1 patient who had a PR on monotherapy. Responses per RECIST v1.1.

CR, complete response; ER, estrogen receptor; HER, human epidermal growth factor; NSCLC, non–small cell lung cancer; PR, partial response; PROC, platinum-resistant ovarian cancer; SCC, squamous cell carcinoma; SCLC, small-cell lung cancer; uPR, unconfirmed PR.

PRESENTED BY:
Ulka Vaishampayan

Conclusions

- Nemvaleukin is a novel cytokine designed to expand the therapeutic potential of high-dose IL-2
  - Design hypothesis confirmed
    - Dose-dependent expansion of $CD8^+$ and NK cells to a level consistent with high-dose IL-2
    - Minimal non–dose-dependent effect on T_{regs}
  - Generally well tolerated, with a manageable safety profile
- Monotherapy activity demonstrated in melanoma and RCC, tumor types in which high-dose IL-2 has proven activity
- Responses observed with nemvaleukin + pembrolizumab in heavily pretreated patients across a range of tumors (including CPI-unapproved and post-CPI failure)
- Data support ongoing global registrational studies
  - ARTISTRY-6: nemvaleukin monotherapy in mucosal and cutaneous melanoma cohorts (poster # TPS9609)
  - ARTISTRY-7: nemvaleukin + pembrolizumab in PROC (poster # TPS5609)

CPI, checkpoint inhibitor; IL-2, interleukin-2; NK, natural killer; PROC, platinum-resistant ovarian cancer; RCC, renal cell carcinoma; T_{reg}, regulatory T cell.

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- Thank you
  - To all the patients who are participating in this study and their families
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EXAMEN sp.z.o.o., Poland
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Korea University Anam Hospital, South Korea
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Hospital Clinico Y Provincial BCN, Spain
MD Anderson Cancer Center Madrid, Spain
Hospital Clinico San Carlos, Spain
START. Hospital Universitario HM Sanchinarro, Spain
Hospital Universitario 12 de Octubre, Spain
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Cleveland Clinic Foundation, USA
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