Poster # TPS9609

ARTISTRY-6: Nemvaleukin Alfa Monotherapy in Patients With Advanced Mucosal and Cutaneous Melanoma

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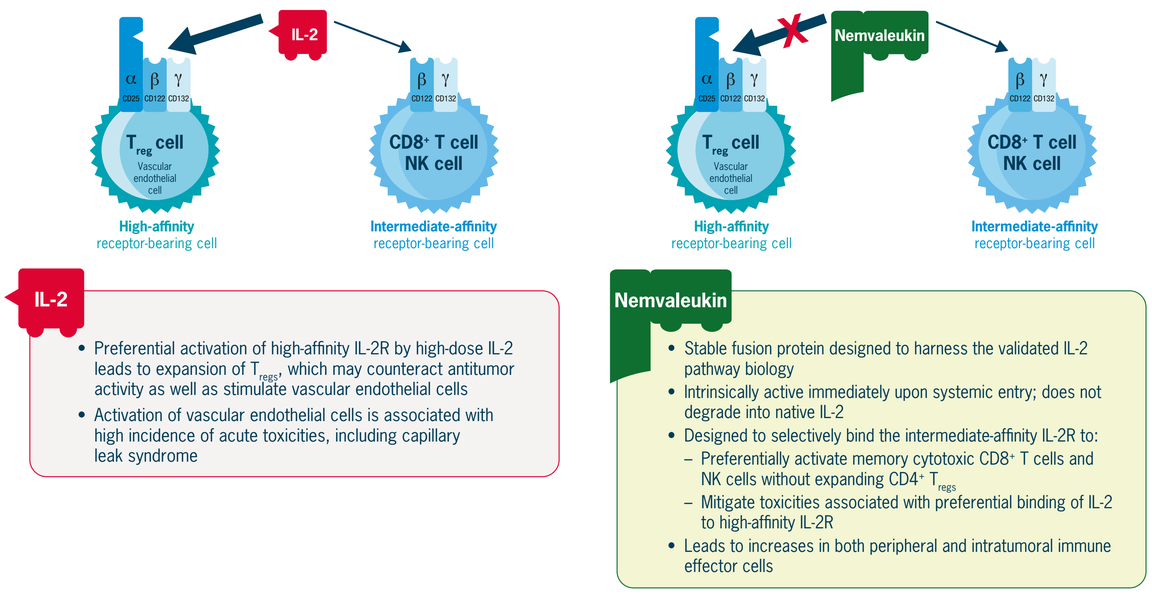
INTRODUCTION

Nemvaleukin alfa (nemvaleukin, ALKS 4230) is a novel, engineered cytokine (Figure 1[1])

- Nemvaleukin has been granted Orphan Drug designation and Fast Track designation for the treatment of mucosal melanoma by the US FDA
- In the ARTISTRY-1 study (NCT02799095), intravenous (IV) nemvaleukin monotherapy at the recommended phase 2 dose (RP2D) of 6 µg/kg demonstrated durable antitumor activity in patients with advanced melanoma, including mucosal melanoma, previously treated with a checkpoint inhibitor (CPI) (Figure 2)[2,3]
  - Additional responses with nemvaleukin monotherapy have been achieved in patients with advanced renal cell carcinoma previously treated with a CPI[2]
  - Nemvaleukin was generally well tolerated, with a low incidence of treatment-related discontinuations[2]
- In the ARTISTRY-2 study (NCT03861793), subcutaneous (SC) nemvaleukin at the RP2D of 3 mg every 7 days (Q7D) demonstrated pharmacodynamic effects consistent with those of IV nemvaleukin[4]

Figure 1: Cell activation by IL-2 and nemvaleukin



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

IL-2, interleukin-2; IL-2R, IL-2 receptor; NK, natural killer; T_{reg}, regulatory T cell.

Advanced cutaneous and mucosal melanoma represent tumor types with vast unmet needs

- Although the introduction of CPIs led to improved outcomes for patients with melanoma, ~50% do not respond to monotherapy and ~40% do not respond to combinations[5]
  - A subset of responders ultimately progress and have limited treatment options, underscoring a high unmet need for novel treatments with durable benefit
- Patients with mucosal melanoma exhibit response rates and progression-free survival times ~2 times lower than those with cutaneous melanoma

Figure 2: Duration of nemvaleukin monotherapy and responses at RP2D in patients with melanoma from ARTISTRY-1 (data cut date 29 October 2021)

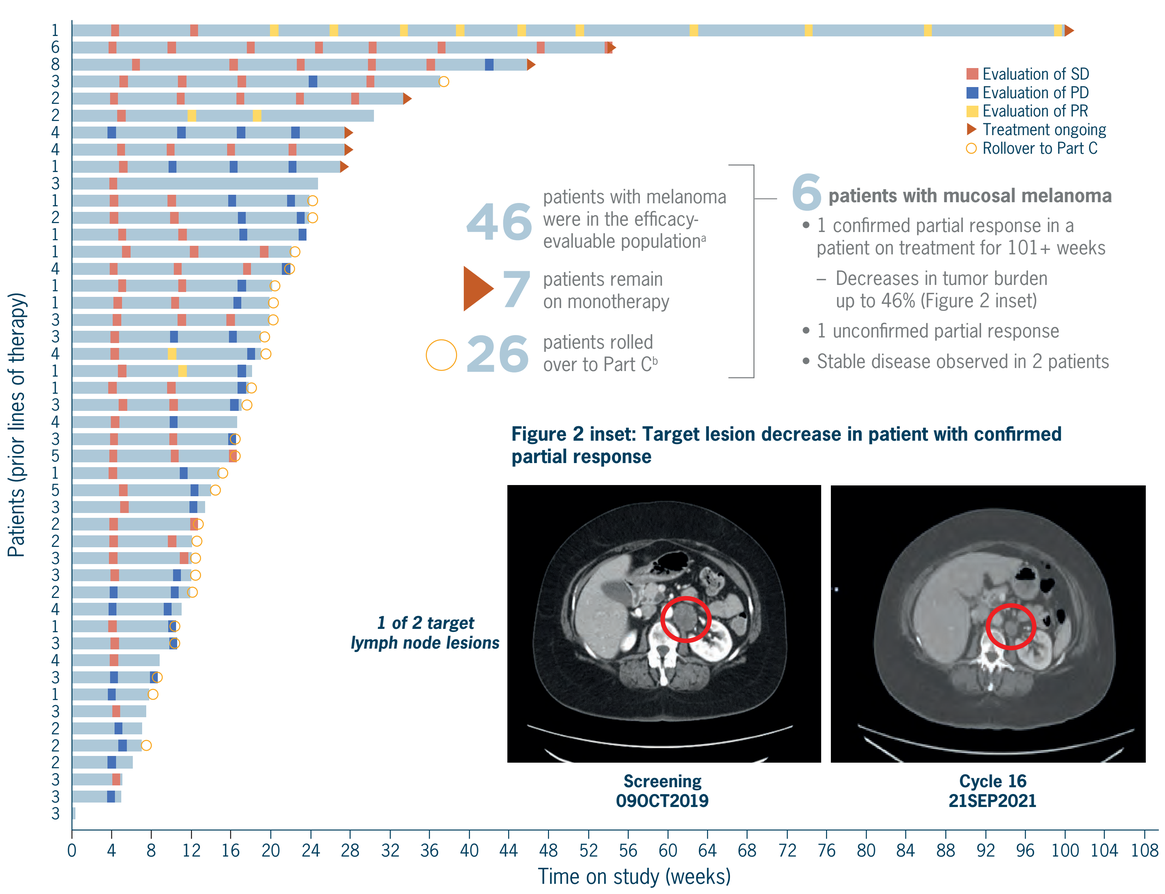


Figure 2 inset: Target lesion decrease in patient with confirmed partial response

PD, progressive disease; PR, partial response; SD, stable disease.
[a]1 patient with mucosal melanoma discontinued prior to first scan (patient request). [b]Part C of the ARTISTRY-1 study is a combination therapy dose expansion cohort (nemvaleukin 3 or 6 µg/kg IV + pembrolizumab 200 mg IV). Patients could roll over to Part C upon progression or stable disease (after ≥4 cycles) on monotherapy.

ARTISTRY-6 STUDY DESIGN

ARTISTRY-6 (NCT04830124) is actively recruiting

An ongoing phase 2, global, multicenter, open-label cohort study of nemvaleukin alfa monotherapy administered subcutaneously in patients with advanced cutaneous melanoma or intravenously in patients with advanced mucosal melanoma who have previously received anti-PD-(L)1 therapy

Patient population

- Adults aged ≥18 years with confirmed diagnosis of unresectable and/or metastatic melanoma
  - Eastern Cooperative Oncology Group performance status of 0 or 1
  - Adequate hematologic reserve and hepatic and renal function
  - Measurable lesion (≥1) that qualifies as a target lesion (Response Evaluation Criteria In Solid Tumors [RECIST 1.1])
- Prior treatment with anti–programmed death (ligand) 1 (PD-[L]1) therapy with or without anti-CTLA-4 therapy
  - With best objective response of partial response or complete response or with stable disease (RECIST 1.1 or iRECIST)
  - Patients with progressive disease may be eligible if they received anti-PD-(L)1 therapy for ≥12 weeks
  - No more than 1 other prior regimen of systemic antineoplastic therapy (eg, targeted therapy, chemotherapy); previous adjuvant and/or neoadjuvant therapy counts as 1 prior regimen
  - Patients with *BRAF* mutations may or may not have received prior targeted therapy
- Prior treatment with talimogene laherparepvec (TVEC) is allowed provided that last exposure to TVEC was ≥28 days prior to first exposure to nemvaleukin and that all injection site reactions to TVEC have resolved
  - TVEC shall not be considered a prior line of systemic antineoplastic therapy, nor shall it be considered a systemic immunomodulatory agent

Cohort 1

(Target N=40)

- Advanced **cutaneous** melanoma
- No more than 5 patients with acral melanoma will be enrolled

Cohort 2

(Target N=70)

- Advanced **mucosal** melanoma

Key exclusion criteria

- Uveal melanoma
- Prior IL-2-based or IL-15-based cytokine therapy
- Exposure, including intralesional, to IL-12 or analogs thereof

Dosing regimen

Cohort 1: nemvaleukin 3 mg SC once Q7D
Cohort 2: nemvaleukin 6 µg/kg IV on days 1-5 followed by 9 days off treatment (cycle 1) or 16 days off treatment (cycle 2+)

Patients will continue to receive nemvaleukin until disease progression or intolerable toxicity

Primary objective

- To evaluate the antitumor activity of nemvaleukin by centralized reviewers' assessment of overall response rate (ORR) based on RECIST 1.1 separately for patients with advanced cutaneous (Cohort 1) and mucosal (Cohort 2) melanoma

Secondary objectives (evaluated separately for Cohort 1 and Cohort 2)

- To evaluate the antitumor activity (other than by centrally assessed ORR), safety, and tolerability of nemvaleukin

Exploratory objectives (evaluated separately for Cohort 1 and Cohort 2)

- To evaluate overall survival, durable and immune durable response rates, and health-related quality of life with nemvaleukin, and pharmacokinetics, immunogenicity, and pharmacodynamic effects of nemvaleukin
- To describe changes in post-treatment patient blood and/or tumor tissue samples and identify properties that may predict response or nonresponse to nemvaleukin monotherapy

REFERENCES AND ACKNOWLEDGMENTS

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ARTISTRY

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