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#6460: First-in-Class Lymphocyte Stimulating Agent (LSA) Nogapendekin Alfa Inbakicept (NAI) Increases Absolute Lymphocyte Count (ALC) in Randomized Trial in Non-Small Cell Lung Cancer (NSCLC)

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BACKGROUND

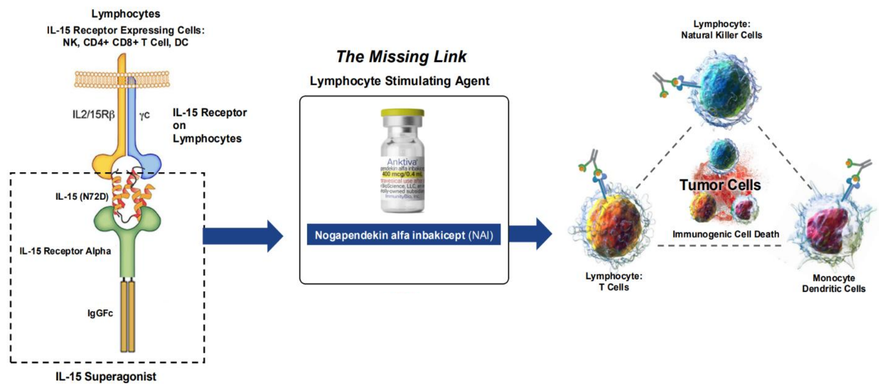
- **Severe lymphopenia (ALC<1,000 cells/μL) significantly lowers overall survival in NSCLC**, is well recognized as a **poor prognostic factor as part of the LIPI (Lung Immune Prognostic Index)** and is associated with the adverse treatment effects of chemotherapy, immunotherapy, and radiation.[1,2]
- Association of ALC levels and mOS suggests that reversing the immune deficit represented by low ALC induced by chemotherapy, radiation, and checkpoint inhibitors may prolong survival across tumor types.
- **Prior to the approval of Nogapendekin alfa inbakicept (NAI),** an IL-15 receptor superagonist which stimulates lymphocytes important in immunogenic cell death (natural killer cells, CD4+ CD8+ T cells and memory T cells)[3], **no treatment existed to address lymphopenia** as measured by the absolute lymphocyte count (ALC) in the CBC differential. Given the MOA, **NAI represents a novel agent with the ability to either prevent of reverse lymphopenia**.
- QUILT-2.023 (NCT NCT03520686) is an open-label randomized controlled study among patients with stage III/IV NSCLC treated in the 1L setting with checkpoint inhibitor (CPI) therapy alone compared to CPI+NAI for participants with PD-L1 ≥1%.[4]

METHODS

- To assess the contribution of effect of NAI as a lymphocyte stimulating agent (LSA) in NSCLC, as previously shown in healthy volunteers[5], comparative analysis was performed between the CPI alone (Control) and CPI+NAI (Experimental) treatment arms in QUILT-2.023.[4]
- ALC from CBC was assessed over 3-week cycles of therapy for the first 10 treatment cycles.
- Statistical analysis to compare ALC values between treatment arms over time was performed using a mixed model for repeated measures of actual ALC values (effects for baseline ALC value, treatment group, time, and group by time interaction); the P-value is from the type III test for the fixed effect of the treatment group.

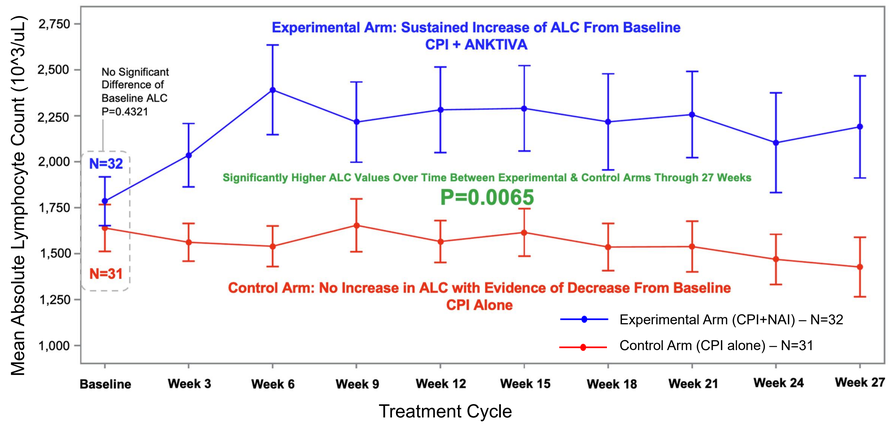
RESULTS

Figure 1: Nogapendekin alfa inbakicept (NAI) Structure & MOA: First-in-class Lymphocyte Stimulating Agent (LSA)



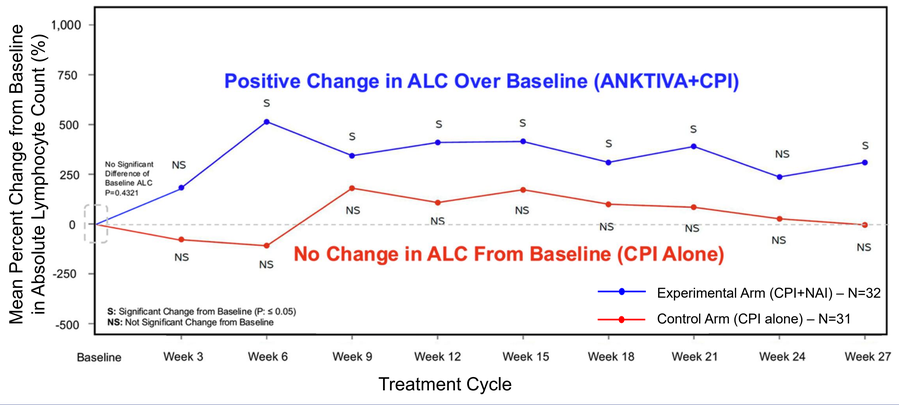
- **Package Insert**: Binding of nogapendekin alfa inbakicept-pmln to its receptor results in proliferation and activation of NK, CD8+, and memory T cells without proliferation of immuno-suppressive Treg cells.[3]

Figure 2: IL-15 Agonist + CPI Increases Mean Absolute Lymphocyte Count



- Compared to CPI alone, the combination of NAI with CPI results in **increase and sustains ALC** over baseline during the course of therapy
- There was no significant difference in baseline mean ALC between the CPI alone and CPI+NAI treatment arms (1.64 cells/mL [range: 0.50-3.69] vs. 1.79 cells/mL [range: 0.60-3.690, respectively) (p=0.4321).

Figure 3: Mean Percent Change from Baseline in Absolute Lymphocyte Count Values Over Time



- **Mean percent change from baseline in ALC for the CPI+NAI treatment arm was elevated and significantly higher** compared to the CPI alone arm over the first 10 treatment cycles (p=0.0065).

CONCLUSIONS

- Analysis of ALC over the first 10 cycles of treatment **demonstrates the ability of NAI to markedly increase ALC soon after starting therapy and sustain those increases over time in patients with NSCLC**.
- These data confirm the findings in normal healthy volunteers[5] that **NAI is the first IL-15 cytokine superagonist in its class to address lymphopenia**.
- The potential of reversing lymphopenia induced by treatment, and prolonging survival, and improving prognosis across tumor types, may be a **paradigm change in cancer care**.

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Disclosures: Dr. Chaitali Nangia has no conflicts of interest to declare.

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