**Results**

- **NX-1607 in Combination with ACT Enhances the Quality of Transferred NX-0255-treated Pmel-1 in the Tumor, Inducing a More Stem Cell-like Memory Phenotype Compared to IL-2**

**Figure 4. NX-1607 in Combination with ACT Enhances the Quality of Transferred NX-0255-treated Pmel-1 in the Tumor, Inducing a More Stem Cell-like Memory Phenotype Compared to IL-2**

- Treatment of CD3-stimulated tumor-specific Pmel-1 cells using NX-0255, a novel small molecule CBL-B inhibitor, is associated with increased anti-tumor activity, increased persistence and memory phenotype in tumor in vivo and following adoptive transfer in an aggressive mouse melanoma model.

- **NX-1607 in combination with ACT enhances the quality of transferred NX-0255-treated Pmel-1 in circulating cells and in tumor, inducing a more memory-like and cytotoxic phenotype compared to IL-2.**

- **The observed antitumor effects of NX-1607 support its potential use in combination with cell-based therapeutics.**

**Conclusions**

- **A Novel Small Molecule Inhibitor of CBL-B Shows Potent Antitumor Activity in Combination with Pmel-1 Adoptive Cell Transfer in an Aggressive Mouse Melanoma Model**

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**A Novel Small Molecule Inhibitor of CBL-B Shows Potent Antitumor Activity in Combination with Pmel-1 Adoptive Cell Transfer in an Aggressive Mouse Melanoma Model**

**Introduction**

-nx-0255: an E3 ubiquitin ligase that is expressed in and regulates immune cells, including T, NK, and dendritic cells

- mice deficient in CBL-B show decreased TH1 cytokine production and reduced T cell-mediated killing of tumor cells

- In T cells, CBL-B inhibits cell activation following TCR engagement, the need of cytokine stimulation

- Inhibiting CBL-B with a small molecule represents a novel strategy to overcome checkpoint resistance and normal tumor activity

- CBL-B inhibiting in vivo treatment of tumor cells: CBL-B could be used as therapy for immune cells that are impaired due to increased tumor activity

- CBL-B inhibiting small molecule can be used in combination with ACT to enhance the quality of transferred Pmel-1 cells

**Background**

**Figure 1. ACT with NX-0255-treated Pmel-1 is Associated with Increased Antitumor Activity, Persistence, and Memory Phenotype**

**Figure 2. ACT Supported by in vivo Treatment with NX-1607 Increases the Antitumor Activity of NX-0255-treated Pmel-1 Cells**

**Figure 3. NX-1607 in Combination with ACT Enhances the Quality of Transferred NX-0255-treated Pmel-1 in Circulating Cells, Inducing a More Memory-like and Cytotoxic Phenotype Compared to IL-2**

**Figure 4. NX-1607 in Combination with ACT Enhances the Quality of Transferred NX-0255-treated Pmel-1 in the Tumor, Inducing a More Stem Cell-like Memory Phenotype Compared to IL-2**

**Figure 5. NX-1607 in Combination with ACT Enhances the Quality of Transferred NX-0255-treated Pmel-1 in the Tumor, Inducing a More Stem Cell-like Memory Phenotype Compared to IL-2**

**Figure 6. NX-1607 in Combination with ACT Enhances the Quality of Transferred NX-0255-treated Pmel-1 in the Tumor, Inducing a More Stem Cell-like Memory Phenotype Compared to IL-2**

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