A Novel Immune Agonist, NKTR-214, Increases the Number and Activity of CD8+ Tumor Infiltrating Lymphocytes in Patients with Advanced Renal Cell Carcinoma

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**Background**

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• Interleukin-2 (IL-2) is a cytokine that activates and expands tumor killing lymphocytes, but also potently induces immunosuppression. A new cytokine therapy, NKTR-214, is emerging as a promising alternative to IL-2.

**Objectives**

- To evaluate the safety and tolerability of NKTR-214 in patients with advanced or metastatic solid tumors
- To assess the immunologic activity of NKTR-214
- To determine the optimal dose to be used in future trials
- To assess the effect of NKTR-214 on clinical outcomes

**Methods**

• Phase 1 trial: 76 patients with advanced renal cell carcinoma (RCC), non-small cell lung cancer (NSCLC), melanoma, or other solid tumors were enrolled
• Dose levels: 0.003, 0.006, and 0.009 mg/kg of body weight every 2 or 3 weeks
• NKTR-214 is a novel, biologic glufosinate analog that binds to the βγ subunit of the IL-2 receptor to induce sustained signaling through the heterodimeric IL-2 receptor pathway

**Results**

- **Safety and Tolerability**
  - 73 patients were treated at a median of 3 cycles
  - 1 patient experienced grade 5 pneumonitis
  - 6 patients (8%) had grade 3/4 adverse events, the most common being fatigue (4%), headache (3%), and nausea (3%)
  - No patients experienced capillary leak syndrome

- **Immunologic Activity**
  - 6 of 15 patients (40%) experienced tumor reductions with single-agent NKTR-214
  - NKTR-214 as a single agent demonstrated a substantial increase in CD8+ T cells in the tumor microenvironment

- **Clinical Outcomes**
  - Of the 6 patients with tumor reduction, 3 patients had complete responses, and 3 patients had partial responses

**Conclusions**

- NKTR-214 as a single agent demonstrated a significant increase in CD8+ T cells in the tumor microenvironment
- NKTR-214 has a favorable safety and tolerability profile
- NKTR-214 was well tolerated in patients with advanced RCC
- NKTR-214 may be a promising new therapy for patients with advanced RCC

**References**