**BACKGROUND**

- Immune system activation with checkpoint inhibitors has proven to be an effective strategy for inhibiting tumor growth and prolonging survival.1
- Anti-PD-1 therapies, such as nivolumab, depend on pre-existing T-cell infiltration within the tumors for optimal efficacy.2
- Abundant and functional tumor-infiltrating lymphocytes are positively linked with tumor response and improved survival with checkpoint inhibitors.3,4

**NKTR-214**

- NKTR-214 is a CD122-biased cytokine agonist conjugated with multiple releasable chains of polyethylene glycol (PEG) designed to provide sustained signaling through the heterodimeric IL-2 receptor pathway (IL-2R) to preferentially activate and expand effector CD8+ T and NK cells over Treg cells.5

**NKTR-214 MONOTHERAPY STUDY**

- A phase 1, multicenter, open-label, dose-escalation study (EXCEL) was conducted to assess the safety, tolerability, efficacy, pharmacokinetics, and pharmacodynamics of NKTR-214 in 28 patients with locally advanced or metastatic solid tumors.6
- Patient recruitment was completed in 15 cycles over 23 months.
- NKTR-214 has a favorable safety and tolerability profile.6-8
- No evidence of immune-mediated AEs or organ-related inflammation (eg, colitis, pneumonitis, dermatitis, hepatitis) was observed.
- Grade 3 hypotension occurred in 14% of patients and was rapidly reversible with IV fluids.

**REFERENCES**


**PIVOT-02 STUDY**

**STUDY OBJECTIVES: NKTR-214 IN COMBINATION WITH NIVOLUMAB**

- Evaluate the immunological effects of NKTR-214 plus nivolumab in combination with nivolumab for optimal efficacy.3,4
- NKTR-214 substantially increased CD8+ T cells that were transiently increased soluble IL-2 receptor alpha (sCD25) from Day 1 to Day 8, shed from activated T cells.
- The personalized treatment with the highest clinical activity for optimal efficacy.
- CD8+ T Cell Proliferation and Selectively Increases T Cells in the Tumor

**ELIGIBILITY FOR ALL DOSE EXPANSION COHORTS**

<table>
<thead>
<tr>
<th>Key Inclusion Criteria</th>
<th>Key Exclusion Criteria</th>
</tr>
</thead>
</table>
| Patients with histologically confirmed diagnosis of Stage III NSCLC treated with a platinum-based chemotherapy regimen for advanced or metastatic disease, or patient refuses standard of care. | Patients are not eligible if they are known to have disease progression on previous therapy or have been treated with a pharmaceutical regimen that has been shown to result in local advanced disease and developed recurrent (local or metastatic) disease within 6 months of completing therapy (are relapsed).
| Patients who received platinum-containing adjuvant, neoadjuvant, or definitive chemoradiation therapy given for locoregional advanced disease and developed recurrent (local or metastatic) disease within 6 months of completing therapy (are relapsed). | Patients who have received, are receiving, or will receive any anti-PD-1, anti-PD-L1, anti-PD-L2, or anti-CTLA-4 antibodies, any other experimental or investigational agents, active immunotherapy, or radiation therapy within 28 days prior to treatment with the study drug.
| Histologically confirmed diagnosis of a locally advanced or metastatic disease of renal cell carcinoma (clear cell, papillary, chromophobe). | Patients who received, are receiving, or will receive any other antibody or drug specifically targeting T cell co-stimulation or checkpoint pathways, indoleamine 2, 3-dioxygenase (IDO), or any other immune suppressor agents.
| Patients who received platinum-containing adjuvant, neoadjuvant, or definitive chemoradiation therapy given for locoregional advanced disease and developed recurrent (local or metastatic) disease within 6 months of completing therapy (are relapsed). | Patients who have a known risk, or are at high risk, for a severe or life-threatening infusion-related reaction.
| Patients with hematopoietic stem cell transplant history limited to a single autologous hematopoietic stem cell transplant who received therapy within 100 days prior to study drug administration. | Patients who have received or are scheduled to receive another investigational agent or device that, in the opinion of the investigator, may interfere with the interpretation of the data or prevent enrollment.
| Patients with hematopoietic stem cell transplant history limited to a single autologous hematopoietic stem cell transplant who received therapy within 100 days prior to study drug administration. | Patients with any prior treatment with a checkpoint inhibitor.
| Patients with a Karnofsky Performance Status > 70. | Patients with a Karnofsky Performance Status ≤ 70.
| Patients with adequate organ function (please refer to the eligibility criteria). | Patients with a history of a serious adverse reaction to the study drug that in the opinion of the investigator is not related to the disease being treated.
| Patients with adequate organ function (please refer to the eligibility criteria). | Patients with any prior treatment with a GIT antibody.
| Patients with a history of a serious adverse reaction to the study drug that in the opinion of the investigator is not related to the disease being treated. | Patients with a history of a serious adverse reaction to the study drug that in the opinion of the investigator is not related to the disease being treated.
| Patients with adequate organ function (please refer to the eligibility criteria). | Patients with any prior treatment with a GIT antibody.
| Patients with a history of a serious adverse reaction to the study drug that in the opinion of the investigator is not related to the disease being treated. | Patients with any prior treatment with a GIT antibody.
| Patients with adequate organ function (please refer to the eligibility criteria). | Patients with a history of a serious adverse reaction to the study drug that in the opinion of the investigator is not related to the disease being treated.
| Patients with adequate organ function (please refer to the eligibility criteria). | Patients with any prior treatment with a GIT antibody.
| Patients with a history of a serious adverse reaction to the study drug that in the opinion of the investigator is not related to the disease being treated. | Patients with any prior treatment with a GIT antibody.
| Patients with adequate organ function (please refer to the eligibility criteria). | Patients with any prior treatment with a GIT antibody.
| Patients with a history of a serious adverse reaction to the study drug that in the opinion of the investigator is not related to the disease being treated. | Patients with any prior treatment with a GIT antibody.

**STUDY DESIGN**

- In the Phase 1 dose-escalation phase, 18 patients were enrolled in the dose-escalation phase. Approximately 250 patients will be enrolled in the expansion phase in five tumor types and eight indications at the recommended phase 2 dose (RP2D).
- All patients will be monitored for treatment response as well as for any side effects.
- Extensive blood and tissue samples are being collected to measure immune activation using immunophenotyping including flow cytometry, immunohistochemistry (IHC), T cell clonality and gene expression.