PROPEL: A Phase 1/2 Trial of NKTR-214 (CD122-Biased Agonist) Combined With Anti-PD-1 (Pembrolizumab) or Anti-PD-L1 (Atezolizumab) in Patients (Pts) With Advanced Solid Tumors

Daniel Cho1, Daniel Vaena2, Jorge M. Chaves3, Nicholas J. Vogelzang4, Marc Matrana5, Matthew Riese6, Mary Tagliaferri7, Jonathan Zalevsky7, Sunny Xie7, Ute Hoch7,


BACKGROUND

- Immune system activation with checkpoint inhibitors has proven to be an effective strategy for inhibiting tumor growth and prolonging survival.1-3
- Anti-PD-1 and anti-PD-L1 therapies, such as pembrolizumab and atezolizumab, depend on pre-existing T cell infiltration within the tumors for optimal efficacy.4-5
- Abundance and functional quality of tumor-infiltrating lymphocytes are positively linked with tumor response and improved survival with checkpoint inhibitors.6-5

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 Tregs (Figure 1)

EXCEL: NKTR-214 MONOTHERAPY (Study Completed)

- Outpatient regimen with continuous IV dosing regimen every 2 or 3 weeks
- Favorable safety and tolerability profile
- No evidence of immune-mediated AEs or organ related inflammation (eg, colitis, pneumonitis, dermatitis, hepatitis, endocrinopathies)
- NKTR-214 substantially increases CD8+ T cells that were newly proliferative (Ki67+) (Figure 2)

PIVOT-02: NKTR-214 PLUS NIVOLUMAB (Active and Enrolling)

- NKTR-214 plus nivolumab resulted in rapid tumor responses in patients with metastatic melanoma, non-small cell lung cancer, and renal cell carcinoma
- NKTR-214 plus nivolumab is safe and tolerable and can be administered as a convenient, outpatient regimen

PROPEL: NKTR-214 PLUS ATEZOLIZUMAB OR PEMBROLIZUMAB (Active and Enrolling)

- Given the early efficacy data and favorable safety profile of NKTR-214 plus nivolumab, PROPEL will evaluate the clinical benefit, safety and tolerability of NKTR-214 combined with pembrolizumab or atezolizumab

PROPEL STUDY (continued)

DESIGN

- In PROPEL (Figure 3), approximately 74 patients with stage III (unresectable) or stage IV melanoma, locally advanced or metastatic urothelial carcinoma (UC), or stage IV non-small cell lung cancer (NSCLC) will be enrolled
- Blood samples for PK analyses will be collected from all patients
- Systemic and tumor tissue-based pharmacodynamic effects of NKTR-214 in combination with pembrolizumab or atezolizumab will be examined
- Tumor measurements will be performed every 8 weeks ± 7 days
- Safety assessments will include AEs, clinical laboratory tests, vital signs, physical examinations, and ECGs

REFERENCES