TPS9596 Poster Session

A randomized phase 2 peri-operative (neoadjuvant plus adjuvant) study of fianlimab (anti–LAG-3) plus cemiplimab (anti–PD-1) versus anti–PD-1 alone in patients with resectable stage III and IV melanoma.

Rodabe Navroze Amaria, Axel Hauschild, Michael Lowe, Janis M. Taube, Adil Daud, Thach-Giao Truong, Sarah A. Weiss, Ankit Mangla, Tapan Miyani, Deidre Williams, Fang Fang, Shuquan Chen, Mark Salvati, Israel Lowy, Rossella Marullo, Matthew G. Fury, Karl Lewis, Humberto Lara-Guerra; The University of Texas MD Anderson Cancer Center, Houston, TX; University Hospital Schleswig-Holstein, Kiel, Germany; Emory University, Atlanta, GA; Johns Hopkins University, Baltimore, MD; University of California San Francisco, San Francisco, CA; Cleveland Clinic, Cleveland, OH; Rutgers Cancer Institute, New Brunswick, NJ; University Hospitals Seidman Cancer Center, Cleveland, OH; Regeneron Pharmaceuticals, Inc., Tarrytown, NY

Background: Prior studies demonstrated use of neoadjuvant plus adjuvant immune checkpoint inhibitors (ICIs) improves event-free survival (EFS) compared with upfront surgery and adjuvant ICI therapy alone, supporting that peri-operative (neoadjuvant plus adjuvant) ICI therapy improves survival outcomes in patients (pts) with clinical stage III and resectable IV melanoma (Mel). Initial efforts in Mel trials to explore combined blockade by anti-programmed cell death-1 (anti–PD-1) and anti-lymphocyte activation gene 3 (anti–LAG-3) antibodies produced incrementally better efficacy than blockade of the PD-1 pathway alone. However, these efforts may not have provided optimal blockade of the two pathways. We have utilized VelocImmune technology to create potentially best-in-class, high-affinity, fully human immunoglobulin G4-blocking antibodies, fianlimab (FIAN; anti–LAG-3) and cemiplimab (CEMI; anti–PD-1). In a multicohort study (NCT03005782), FIAN + CEMI demonstrated reproducibly high clinical activity (objective response rate [ORR]: 57%; median progression-free survival: 24 months; N=98) in three independent cohorts of pts who were naïve to anti–PD-1 treatment in the advanced Mel setting, with an acceptable safety profile. Thus, the combination of FIAN + CEMI warrants an investigation as a peri-operative regimen in resectable, clinically detectable, high-risk, stage III and IV cutaneous Mel. **Methods:** This is a randomized Phase 2 peri-operative study (NCT06190951) in pts with clinical stage III/IV Mel with resectable disease. Pts will receive 3 cycles of neoadjuvant therapy followed by complete surgical resection, and continue with an optional 15 cycles of adjuvant therapy, based on pathological response. The primary objective is to compare the effect of FIAN + CEMI versus CEMI alone as measured by the pathological complete response (pCR) rate. Approximately 150 pts will be randomized 1:1:1 to three arms (intravenously once every 3 weeks): Arm A, CEMI 350 mg + placebo; Arm B, High Dose FIAN + CEMI 350 mg; Arm C, Low Dose FIAN + CEMI 350 mg. Pts will be stratified based on tumor, node, metastasis (TNM) stage and geographical region. Key inclusion criteria: age ≥18 years; resectable clinical stage III/IV histologically confirmed Mel; pts with stage III Mel must have clinically detectable disease; Eastern Cooperative Oncology Group performance status 0 or 1; adequate bone marrow, hepatic, and kidney function. The primary endpoint is pCR rate by blinded independent pathological review performed centrally. The secondary endpoints are pCR rate (by local assessment), major pathological response (by local and central review), EFS, overall survival, distant metastasis-free survival, relapse-free survival, ORR, safety, pharmacokinetics, immunogenicity, and patient-reported outcomes. Clinical trial information: NCT06190951. Research Sponsor: Regeneron Pharmaceuticals, Inc.; NA.