T-1

Safety, Pharmacodynamic, and Antitumor Activity of Tidutamab, an SSTR2 x CD3 Bispecific Antibody, in Subjects with Advanced Neuroendocrine Tumors

Bassel F. El-Rayes[1], Andrew E. Hendifar[2], Shubham Pant[3], Breelyn A. Wilky[4], Matthew J. Reilley[5], Al B. Benson[6], Warren A. Chow[7], Bhavana Konda[8], Jason Starr[9], Daniel H. Ahn[10], Pamela L. Kunz[11], Jonathan R. Strosberg[12], Jennifer R. Eads[13], Kimberly J. Perez[14], Nitya P. Raj[15], George A. Fisher[16], Sowmya Chollate[17], Catherine A. Fleener[17], Ying Ding[17], Zequn Tang[17]

[1]Winship Cancer Institute at Emory University, Atlanta, GA; [2]Cedars-Sinai Medical Center, Los Angeles, CA; [3]The University of Texas MD Anderson Cancer Center, Houston, TX; [4]University of Colorado Anschutz Medical Campus, Aurora, CO; [5]University of Virginia School Of Medicine, Charlottesville, VA; [6]Lurie Cancer Center, Chicago, IL;< sup>[7]City of Hope National Medical Center, Duarte, CA; [8]Ohio State University Medical Center, Columbus, OH; [9]Mayo Clinic, Jacksonville, FL; [10]Mayo Clinic Hospital, Phoenix, AZ; [11]Stanford Cancer Center, Stanford, CA; [12]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; [13]Hospital of the University of Pennsylvania, Philadelphia, PA; [14]Dana Farber/Harvard Cancer Center, Boston, MA; [15]Memorial Sloan Kettering Cancer Center, New York, NY;< sup>[16]Stanford Cancer Center, Palo Alto, CA; [17]Xencor, Inc., San Diego, CA

BACKGROUND: Somatostatin receptor 2 (SSTR2) is overexpressed in neuroendocrine tumors (NETs), gastrointestinal stromal tumors (GIST), and other cancers. Tidutamab is a humanized, anti-SSTR2 x anti-CD3 bispecific antibody that directs T-cell-mediated cytotoxicity to SSTR2+ cells.

METHODS: This Phase 1 study (NCT03411915) investigates the safety/tolerability and maximum tolerated dose (MTD) of tidutamab, administered as weekly infusions in 28-day cycles, in parallel cohorts of advanced NET and GIST subjects. We report updated safety, pharmacodynamic, and response (RECIST 1.1) data for NET cohorts.

RESULTS: As of 16 Jun 2021, 41 subjects (median age, 64 years; 46% male) were treated: 21 in dose escalation and 20 in expansion at the MTD (first dose, 0.3µg/kg, 1.0µg/kg thereafter); 1 subject remains on treatment. Grade 3 treatment-related adverse events in ≥2 subjects included nausea and vomiting (14.6%); diarrhea (9.8%); anemia (7.3%); and fatigue, malnutrition, oesophagitis, esophageal dysmotility, and cytokine release syndrome (4.9%). Grade 3/4 treatment-related laboratory abnormalities (≥3 subjects) included lymphopenia (29.3%); transaminase elevation and GGT increase (19.5%); hypophosphatemia (9.8%); and lipase increase (7.3%). Among 41 subjects, median progression-free survival was 8.2 months (95% CI 2.7, 14.3). The KM estimate of median overall survival (OS) was 15.5 months; OS at 12 months was 77%. The best response was stable disease (11/20 evaluable subjects; 55%). Among 11 subjects with stable disease, median duration was 3 months. Tidutamab induced acute/sustained T-cell activation and cytokine release. Higher baseline CD4 central memory cells were positively associated with stable disease >6 months, while higher baseline intratumoral PDL1 and on-treatment increases in peripheral T-cell PD1 expression were associated with shorter time on study.

CONCLUSION: Tidutamab was generally well tolerated with disease control in >50% of evaluable NET subjects. Additional studies in other tumors that express SSTR2 are warranted, and poor outcomes in subjects with higher PD(L)-1 expression suggest combinations with checkpoint inhibitors should be considered.

ABSTRACT ID: 109