408 PRELIMINARY BIOMARKER AND CLINICAL ATA OF A PHASE 2A STUDY OF NT-I7, A LONG-ACTING INTERLEUKIN-7, PLUS PEMBROLIZUMAB: COHORT OF SUBJECTS WITH CHECKPOINT INHIBITOR-NAÏVE ADVANCED PANCREATIC CANCER

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Background Pancreatic cancer (PaC) is immune-quiescent and resistant to single-agent checkpoint inhibitor (CPI). NT-I7 (efineptakin alfa) is the first-in-class long-acting IL-7 that can increase T-cell infiltration in the tumor microenvironment (TME) and may enhance tumor responsiveness to CPI therapy. We hypothesize that the combination of NT-I7 and pembrolizumab may result in enhanced efficacy in CPI-naïve advanced PaC.

Methods This is an open-label, phase 2a, study in subjects with relapsed/refractory (R/R) tumors, including CPI-naïve R/R PaC. Subjects received NT-I7 intramuscularly at 1200 µg/kg every 6 weeks (Q6W) plus pembro 200 mg intravenously Q3W. Antitumor activity based on Overall Response Rate (ORR) was assessed by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. Biomarker analyses of peripheral blood and tumor biopsies were performed.

Results As of 15-July-2021, 26 subjects were enrolled in the CPI naïve R/R PaC cohort. Median age 69 years [31–81], ECOG PS 0 (35%), 1 (65%). Twenty-one (81%) subjects had $\geq$ 2 prior therapies All subjects had metastatic or locally advanced disease at enrollment. The median duration of follow-up was 3.3 months. Among 10 subjects with at least 1 post-treatment tumor assessment, the RECIST1.1-based ORR and disease-control rate (DCR) were 10% and 50%, respectively. One subject with MSS and TMB of 1, achieved a confirmed partial response (cPR) with 65% tumor reduction and drastically improving CA19-9. Treatment-related adverse events (AEs) occurred in 14 (53.8%) subjects, 9 (34.6%) G1–2, 3 (11.5%) G3; 2 (7.7%) G4; no G5 AEs were reported. No subjects discontinued from treatment due to AE. NT-I7 + pembro elicited a significant increase in the peripheral absolute lymphocyte count that peaked at week 3 (>3X from baseline, $p<0.0001$) and was sustained at least until week 18. CD4+/CD8+ T-cells subsets followed the same response pattern. Importantly, Stem-Cell Memory CD8+ T-cells (TSCM), the potential target for CPI, were markedly increased (>15X, $p<0.05$) post-study treatment. The CD8+ Effector-to-Treg ratio and plasmatic chemokines (CXCL9, CXCL10, CXCL11 and CCL9) were also significantly increased. The cPR subject had enhanced T-cell infiltration in the TME at week 5. Subject's follow-up continues and updated data will be presented.

Conclusions The chemo-free combination of NT-I7 + pembro was well tolerated and showed promising anti-tumor activity in subjects with CPI-naïve R/R PaC. Increased TSCM and CD8+ T-cell infiltration within TME may be the underlying mechanisms of action for the observed efficacy. These results support continued evaluation of NT-I7 + pembro in subjects with CPI-naïve R/R PaC.

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Trial Registration NCT04332653

Ethics Approval The trial was approved by MD Anderson IRB (#2020–0008_MOD001), Mary Crowley IRB (#20–13) and Advarra IRB (#Pro00042639)All participant gave informed consent prior to study enrollment.

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