# T-2

# A Pilot Study of Pembrolizumab and Liver-Directed Therapy for Patients with Well-Differentiated Neuroendocrine Tumors and Symptomatic and/or Progressive Liver Metastases

***Nicholas Fidelman*[1]*;*** *Emily Bergsland*[1]*; Lawrence Fong*[1]

[1]*University of California San Francisco*

**BACKGROUND:** Well-differentiated neuroendocrine tumors (WD-NET) have a relatively low tumor mutation burden and do not commonly express the programmed death ligand 1 (PD-L1), characteristics. The intensity of anti-tumor immune response, can potentially be enhanced by addition of liver-directed therapy (LDT), such as thermal ablation or embolization against one or several of the lesions. This pilot study aims to evaluate whether combining pembrolizumab with LDT results in abscopal effects for patients with WD-NET.

**METHODS:** Design: This is a four-arm, open-label non-randomized pilot study in biomarker "unselected" patients with metastatic WD-NET. All patients will be treated with pembrolizumab. LDT will be administered during cycles 1 and 5. Patients with up to 6 liver lesions (largest up to 4 cm) will be treated with radiofrequency ablation (n=8) or cryoablation (n=8). Patients with up to 75% liver parenchyma replacement by tumor and largest lesion up to 5 cm will be treated with subsegmental embolization (n=8). Patients with up to 75% liver parenchyma replacement by tumor and largest lesion larger than 5 cm will be treated with subsegmental Yttrium-90 radioembolization (n=8). Key eligibility: Metastatic functional or non-functional WD-NET of any grade from any site with at least one symptomatic and progressive liver lesion over 12 months. No prior

immunotherapy, radiation, or LDT. Bilirubin and creatinine ≤1.5x ULN, ECOG PS 0-1, agreeable to baseline and on-treatment tumor biopsies.

**RESULTS:** Treatment: Pembrolizumab 200mg IV Q21 days for up to 35 treatments. LDT with pembrolizumab cycles 1 and 5. Primary endpoint (EP): Incidence of abscopal response (by RECIST v. 1.1) to pembrolizumab in combination with LDT. Secondary EP: Safety, duration of response, progression-free survival. Exploratory EP: PD-L1 expression before and after LDT, relationship between blood and tissue immune profile, Ki-67 index and response to therapy. Current enrollment: 0 of 32 patients enrolled. Clinical trial registry number: NCT03457948