C-19

Phase 2 Trial of Pembrolizumab-based Therapy in Previously Treated Extrapulmonary Poorly-differentiated Neuroendocrine Carcinomas: Results of Part B (Pembrolizumab Plus Chemotherapy)

Jennifer A. Chan[1], Nitya P. Raj[2], Rahul R. Aggarwal[3], Thomas A. Hope[3], K. Pallav Kolli Kolli[3], Li Zhang[3], Delaire Fattah[3], Susan Calabrese[3], Jennifer A. Grabowsky[3], Kimberly Perez[1], Sofia Von Fedak[1], April DeMore[2], Pamela N. Munster[3], Mallika Dhawan[3], Diane Reidy-Lagunes[2], Lawrence Fong[3], Emily K. Bergsland[3]

[1]Dana-Farber Cancer Institute, Boston, MA; [2]Memorial Sloan Kettering Cancer Center, New York, NY; [3]University of California San Francisco, San Francisco, CA

BACKGROUND: The efficacy of immune checkpoint inhibitor therapy has not been established in extrapulmonary poorly-differentiated neuroendocrine carcinomas (EP-PDNECs). We investigated the efficacy and safety of pembrolizumab (PEM)-based therapy in biomarker-unselected patients with EP-PDNECs. In Part A, PEM alone was inactive (ASCO GI 2019). We now report the results of Part B (PEM plus chemotherapy).

METHODS: We conducted an open label, multicenter, phase 2 study of PEM-based therapy in patients with EP-PDNECs with disease progression on first-line systemic therapy. Patients were treated with PEM 200 mg IV every 3-week cycle plus dealers' choice chemotherapy: weekly irinotecan (IRI, 125 mg/m2 day 1,8 of every 21-day cycle) or weekly paclitaxel (PAC, 80 mg/m2). After a PEM/IRI safety lead-in (N=6), 16 additional patients were enrolled. Primary endpoint was objective response rate (ORR) by RECIST 1.1. Secondary endpoints included safety, overall survival (OS), and progression-free survival (PFS).

RESULTS: Of 22 patients enrolled: male/female 15/7; median age 57 years (range 34-75); ECOG PS 0/1: 10/12; histology: 6 large cell, 8 small cell, 3 mixed, 5 NOS. Primary site: GI 50%, pancreas/biliary 23%, GYN 5%, unknown 23%. Chemo choice: 17 IRI and 5 PAC. Median cycles of therapy administered was 3 (range 0-13). Treatment-related Gr 3-4 AE occurred in 8 patients. Gr 3 AE attributed to PEM included fatigue, pain, ALT increase, nausea, fever. Grade 3-4 AE attributed to chemo included fatigue, neutropenia, diarrhea, pain, ALT increase, nausea. ORR was 5%: PR in 1 patient (5%), SD 4 (18%), PD 13 (59%); 4 (18%) unevaluable. Median PFS 2 mo. Median OS 4 mo. Reasons for treatment discontinuation in 21 patients included PD (76%), AE (10%), withdrawal of consent/other therapy (14%).

CONCLUSION: PEM + chemotherapy was not effective in this pretreated, biomarker-unselected population of EP-PDNECs arising in different organs. Biomarker studies are planned. Clinical trial information: NCT03136055.

ABSTRACT ID: 172