Treatement with pemblorizumab in combination with the oncolytic virus pelareorep promotes anti-tumor immunity in patients with advanced pancreatic adenocarcinoma

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Abstract

Background: Pemblorizumab is an intravenously delivered oncolytic reovirus that can induce a T cell-inflamed phenotype in pancreatic ductal adenocarcinoma (PDAC). In prior studies, tumor tissue analysis from patients treated with pemblorizumab showed pelareorep replication, increased CD8+ T cell infiltration, and upregulation of PD-L1. We hypothesized that pemblorizumab in combination with pembrolizumab in patients with PDAC would lead to improved responses and anti-tumor immunological changes within peripheral blood and tumor biopsies in responding patients.

Methods: PDAC patients who progressed after first-line treatment received pemblorizumab at a dose of 4.5x10^{10} TCID_50 IV on days 1, 3, 5, 7, 9, 11, 13, 15, and 17 & 19 onwards. Pemblorizumab was administered on day 1 of each 21-day cycle at 200 mg IV. The primary objective was overall response rate by RECIST v 1.1 criteria. Secondary objectives included evaluating immune infiltrates within tumor tissue and peripheral blood, performed by multi-plex immunohistochemistry and spectral flow cytometry (Cytek), respectively.

Results: Thirteen patients were enrolled. Disease control was achieved in 42% of the 12 efficacy-evaluable patients. One patient achieved a partial response (PR). Four additional patients achieved stable disease (SD). This phase 2 study (NCT03723915) enrolled PDAC patients who progressed after first line chemotherapy and unselected PDAC population. Additional correlation analyses between treatment efficacy and immunological changes will be presented. The anti-tumor activity of pemblorizumab and checkpoint blockade therapy is being evaluated further in ongoing studies.

Background and Rationale

In prior studies, pemblorizumab and pembrolizumab did not add significant toxicity to chemotherapy and showed encouraging efficacy in second line PDAC patients. Prior studies in first-line PEMBA achieved encouraging 1 & 2 year-survival rates of 46% & 24%, respectively, with chemotherapy and pemblorizumab treatment (1,2). On-treatment biopsies have shown that pemblorizumab induced an inflammatory phenotype in the tumor micro-environment that facilitates synergy with checkpoint blockade therapy (see pemblorizumab mechanism of action, Fig 1(3,4). We hypothesized that pemblorizumab in combination with pembrolizumab in patients with PDAC would lead to improved responses and anti-tumor immunological changes within peripheral blood and tumor biopsies in responding patients.

Methods

- This phase 2 study (NCT03723915) enrolled PDAC patients who progressed after first line treatment. Patients received therapy until disease progression or unacceptable toxicity as follows: pelareorep (4.5x10^{10} TCID_50 IV) plus pembrolizumab (200 mg IV) for 21 days. The annual overall response rate by RECIST v 1.1 criteria. Secondary objectives included evaluating immune infiltrates within tumor tissue and peripheral blood, performed by multi-plex immunohistochemistry and spectral flow cytometry (Cytek), respectively.

Results

Figure 2. Study Schedule.