Format: Abstract

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Durvalumab With or Without Tremelimumab for Patients With Metastatic Pancreatic Ductal Adenocarcinoma: A Phase 2 Randomized Clinical Trial.

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Abstract

IMPORTANCE: New therapeutic options for **patients** with **metastatic** pancreatic ductal adenocarcinoma (mPDAC) are needed. This study evaluated dual checkpoint combination therapy in **patients** with mPDAC.

OBJECTIVE: To evaluate the safety and efficacy of the anti-PD-L1 (programmed death-ligand 1) antibody using either **durvalumab** monotherapy or in combination with the anticytotoxic T-lymphocyte antigen 4 antibody using **durvalumab** plus **tremelimumab** therapy in **patients** with mPDAC.

DESIGN, SETTING, AND PARTICIPANTS: Part A of this multicenter, 2-part, phase 2 randomized clinical trial was a lead-in safety, open-label study with planned expansion to part B pending an efficacy signal from part A. Between November 26, 2015, and March 23, 2017, 65 **patients** with mPDAC who had previously received only 1 first-line fluorouracil-based or gemcitabine-based treatment were enrolled at 21 sites in 6 countries. Efficacy analysis included the intent-to-treat population; safety analysis included **patients** who received at least 1 dose of study treatment and for whom any postdose data were available.

INTERVENTIONS: Patients received **durvalumab** (1500 mg every 4 weeks) plus **tremelimumab** (75 mg every 4 weeks) combination therapy for 4 cycles followed by **durvalumab** therapy (1500 mg every 4 weeks) or **durvalumab** monotherapy (1500 mg every 4 weeks) for up to 12 months or until the onset of progressive disease or unacceptable toxic effects.

MAIN OUTCOMES AND MEASURES: Safety and efficacy were measured by objective response rate, which was used to determine study expansion to part B. The threshold for expansion was an objective response rate of 10% for either treatment arm.

RESULTS: Among 65 randomized **patients**, 34 (52%) were men and median age was 61 (95% CI, 37-81) years. Grade 3 or higher treatment-related adverse events occurred in 7 of 32 **patients** (22%)

receiving combination therapy and in 2 of 32 **patients** (6%) receiving monotherapy; 1 patient randomized to the monotherapy arm did not receive treatment owing to worsened disease. Fatigue, diarrhea, and pruritus were the most common adverse events in both arms. Overall, 4 of 64 **patients** (6%) discontinued treatment owing to treatment-related adverse events. Objective response rate was 3.1% (95% CI, 0.08-16.22) for **patients** receiving combination therapy and 0% (95% CI, 0.00-10.58) for **patients** receiving monotherapy. Low patient numbers limited observation of the associations between treatment response and PD-L1 expression or microsatellite instability status.

CONCLUSION AND RELEVANCE: Treatment was well tolerated, and the efficacy of **durvalumab** plus **tremelimumab** therapy and **durvalumab** monotherapy reflected a population of **patients** with mPDAC who had poor prognoses and rapidly progressing disease. **Patients** were not enrolled in part B because the threshold for efficacy was not met in part A.

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