Phase 2 trial of the indoleamine 2,3-dioxygenase (IDO) inhibitor indoximod plus gemcitabine / nab-paclitaxel for the treatment of metastatic pancreas cancer: interim analysis

INTRODUCTION

• Pancreatic cancer is the 4th leading cancer death rate, and 5th leading cause of cancer death. The 5-year survival rate is 7%.
• Current standard-of-care chemotherapy (gemcitabine and nab-paclitaxel) for patients with metastatic cancer has a limited benefit over best supportive care (BSC) in terms of median overall survival (OS) and median progression-free survival (PFS).

METHODS

Study Design and Assessments

• Phase 2, single arm, open-label study
• Phase 2 dose of indoximod (1200 mg orally twice daily [BID]) continuous dosing
• Gemcitabine (1000 mg/m2 given intravenously on Days 1, 8, and 15 of 28-day cycles) and nab-paclitaxel (125 mg/m2 given intravenously on Days 1, 8, and 15 of 28-day cycles) were administered in combination with indoximod.
• Patients continued treatment until they experienced disease progression or significant toxicity

RESULTS

• A Phase 1/2, single arm, open-label trial was initiated to show long-term in 4-month cycles. No protocol-defined endpoints are available at the following 6-month mark.
• Responses data available to patients at times of clinical cutoff are 80% of the overall cohort.
• Elderly patients (≥ 70 years of age) were included in this analysis.
• Overall, 31 evaluable patients were included in this analysis.

Safety and Tolerability

• The combination regimen was well tolerated.
• The most frequent (≥ 20%) of all-grade adverse events occurring in ≥ 10% of patients were: anemia (25%), nausea/vomiting (23%), fatigue (22%), and diarrhea (20%).
• Grade 3 or 4 adverse events occurring in ≥ 10% of patients were: anemia (22%), proteinuria (9%), and fatigue (8%).
• All grade 4 laboratory abnormalities were resolved.

Eligibility

• Patients ≥ 18 years of age with histologically or cytologically confirmed metastatic adenocarcinoma of the pancreas
• Karnofsky performance status ≥ 70
• Life expectancy > 3 months
• Patients must have received prior chemotherapy, surgery, chemotherapy or immunotherapy for the treatment of metastatic disease

OBJECTIVES

• Primary endpoint for Phase 2b: Overall Survival
• Secondary endpoints
• Objective response rate
• Progression-free survival

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CONCLUSIONS

• The combination of indoleamine 2,3-dioxygenase (IDO) inhibitor indoximod plus gemcitabine / nab-paclitaxel in the Phase 2 trial demonstrated a favorable safety profile and encouraging response rate in patients with metastatic pancreas cancer.
• In addition, the combination achieved a high rate of tumor shrinkage, which is suggestive of an immune-mediated mechanism of action.

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REFERENCES


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The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.