Pancreatic cancer is fatal malignant tumor with low resection rate and poor prognosis. We aimed to assess the safety and efficacy of a new mode of induction therapy for patients with potentially resectable pancreatic cancer (RPC).

Gemcitabine (1000 mg/m2) and nab-paclitaxel (125 mg/m2; AG) were administered to patients with LAPC or BRPC on days 1 and 8, along with tislelizumab (200 mg) on day 1 intravenously (IV) every three weeks. Concurrently, the patients underwent stereotactic body radiotherapy (SBRT) with simultaneous integrated boost (SIB) during the third cycle of treatment. Surgical intervention was reassessed after four cycles of treatment. We then analyzed the objective response rate (ORR), R0 resection rate, median overall survival (mOS), median progression-free survival (mPFS), and safety. Plasma biomarkers associated with clinical response were investigated as exploratory objectives.

In total, 25 patients were enrolled. At the end of the last follow-up (July 31, 2022), the ORR was 60%, 10 patients underwent resection, and the R0 resection rate was 90%. The disease control rate (DCR) was 100%. Two of the ten resected patients achieved pathologic complete response (pCR) and one patient achieved major pathological response (MPR). The mPFS, 12-months PFS rate, and 12-months OS rate were 13.7 months (95% CI: 12.4–NR), 68% (95% CI: 51.97%–88.98%), and 72.63% (95% CI: 56.04%–94.14%), respectively.

No severe postoperative complications were observed. Grade 3 or higher hematologic toxicities were mainly anemia (8%) and thrombocytopenia (8%). Major non-hematologic toxicity was jaundice.

Biomarker analysis indicated that patients with continuous carbohydrate antigen 19-9 decline and elevated peripheral blood eosinophil counts during treatment exhibited better survival outcomes.

Furthermore, circulating tumor DNA (ctDNA) analysis revealed that patients with a >50% decline in maximal somatic variant allelic frequency (maxVAF) between the first clinical evaluation and baseline had a longer survival outcome and higher response rate than those who did not (PFS: not reached vs. 10.6 months, p = 0.035; OS: not reached vs. 13.2 months, p = 0.0076; ORR: 88.9% vs. 35.7%, p = 0.028). Moreover, maxVAF decline (>50%) significantly improved the surgical rate after induction therapy (70.0% vs. 27.2%; p = 0.035).

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Anti-PD-1 inhibitor tislelizumab plus AG chemotherapy followed by concurrent SBRT with SIB provided remarkable efficacy with reasonable tolerability as induction therapy for patients with BRPC and LAPC.