P-4 Efficacy and safety of sintilimab combined nab-paclitaxel and gemcitabine as first-line treatment for metastatic pancreatic ductal adenocarcinoma (PDAC): A retrospective analysis

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Background: Advanced pancreatic cancer is a devastating disease with a short survival time. Chemotherapy is one of the most important treatments for advanced pancreatic cancer, which has a synergistic mechanism with immunotherapy on the basis of theory. Exploring more effective combination regimens based on immunotherapy is a research hotspot in recent years. We evaluated the efficacy and safety of sintilimab combined with nab-paclitaxel/gemcitabine as first-line treatment to provide new evidence for chemotherapy combined immunotherapy of advanced PDAC.

Methods: This was a retrospective study in patients with advanced PDAC performed from September 20, 2020 to February 10, 2022. Patients who received first-line sintilimab plus nab-paclitaxel/gemcitabine treatment were enrolled. The primary end point was progression free survival (PFS). Secondary end points included objective response rate (ORR), disease control rate (DCR), and safety.

Results: A total of 20 patients were eligible for response assessment. In the general population, complete response (CR) was not observed, 6 patients achieved partial response (PR), 12 patients had stable disease (SD) and 2 patients had progression disease (PD). The ORR and DCR were 6(30%) and 18(90%), respectively. Median PFS was 5.2 months(95%CI:2.916-7.484).The most common grade 3 treatment related AEs (trAEs) were hematological toxicity, however, the incidence is $\leq$10%, anemia(10%), leukopenia(10%), neutropenia(10%), thrombocytopenia(5%).Non-hematological toxicity were hand-foot syndrome(10%) and nausea(10%). Only one patient had grade 4 oral mucositis.

Conclusions: Sintilimab combined with nab-paclitaxel and gemcitabine can be used a feasible first-line treatment strategy for patients with metastatic pancreatic cancer, and the toxicity is tolerable. More data are needed in the future to explore the correlation between biomarkers and efficacy and to identify people who can benefit from combined strategy.

Legal entity responsible for the study: The author.

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P-5 Phase II study (daNIS-1) of the anti-TGF-β monoclonal antibody (mAb) NIS793 +/- spartalizumab in combination with nab-paclitaxel/gemcitabine (NG) versus NG alone in patients with first-line metastatic pancreatic ductal adenocarcinoma (mPDAC)

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Background: Overall survival remains low for patients (pts) with mPDAC despite approved therapies, highlighting the need for further innovative treatment options. Intra-tumoral fibrosis that characterizes PDAC has been associated with a state of immune exclusion and may constitute a mechanical obstacle to the intra-tumoral penetration of chemotherapy as well as contribute to the lack of efficacy of immunotherapy. TGF-β plays a key role in regulating the tumor microenvironment and emerging evidence points to its role as a pivotal activator of cancer-associated fibroblasts, leading to the development of fibrotic networks. Preclinical data in murine models have shown that TGF-β blockade augmented the antitumor activity of both NG and anti-PD-1 therapy, leading to tumor regression. These data provide the rationale for combining TGF-β-targeting agents with immunotherapy and chemotherapy. NIS793 is a human IgG2 mAb that binds to TGF-β. This study investigates NIS793 with and without spartalizumab (PD-1 antagonist) combined with NG in treatment naïve mPDAC.

Trial design: This is a phase II open-label, randomized, multicenter study (NCT04390763) beginning with a safety run-in period followed by randomization. Eligible pts are adults with previously untreated mPDAC and ECOG performance status score $\leq$1. Pts are excluded if they have a microsatellite-unstable tumor. The safety run-in data will be analyzed after $\geq$6 pts have received NIS793 (intravenously [IV] 2100 mg Q2W) + spartalizumab (IV 400 mg Q4W) + nab-paclitaxel (IV 125 mg/m2 on Days 1, 8 and 15) + gemcitabine (IV 1000 mg/m2 on Days 1, 8 and 15) for 1 cycle (28 days) to assess the safety and tolerability of the combination. In the randomized part, pts will be randomized 1:1:1 to NIS793 + spartalizumab + NG (n=50) or NIS793 + NG (n=50) or NG (n=50). Treatment will continue until unacceptable toxicity, disease progression, discontinuation by investigator's/pt's choice, or withdrawal of consent. The primary objective is to evaluate the progression-free survival per RECIST 1.1, of NIS793 + NG $\pm$ spartalizumab versus NG alone. Secondary objectives include safety and tolerability, antitumor activity, overall survival, change in tumoral CD8 and PD-L1 status, and characterization of immunogenicity and pharmacokinetics. Efficacy will be assessed locally per RECIST v1.1 and iRECIST at screening, every 8 weeks for 1 year and then every 12 weeks until disease progression. Blood and tumor samples will be taken at baseline and during study treatment for pharmacokinetic, immunogenicity and biomarker assessments. This study is ongoing and will enroll pts from 31 sites across 14 countries. The first pt was treated on October 22, 2020. Enrollment for the randomized part of the study started on August 09, 2021.

Clinical trial identification: NCT04390763.

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P-6 Prognostic value of the lymphocyte/monocyte ratio in advanced pancreatic cancer

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Background: Several studies have evaluated the interest of inflammatory markers as prognostic indicators for pancreatic cancer. The aim of this work was to investigate the utility of the lymphocyte/monocyte ratio (LMR) as a prognostic factor in Tunisian advanced pancreatic cancer.