

Tolerability of Nab-Paclitaxel Plus Gemcitabine as Adjuvant Setting in Japanese Patients With Resected Pancreatic Cancer

Phase I Study

SUPPLEMENTAL DIGITAL CONTENT

SUPPLEMENTARY TABLE 1. Complete Inclusion Criteria

Written informed consent has been obtained from the subject to participate in the clinical trial

Age: 20 to <80 years at the time of informed consent

Histologically confirmed invasive pancreatic ductal carcinoma

Macroscopically complete resection of the primary pancreas

- Residual degree of local cancer is R0 or R1

TNM staging* is T1–3, N0–1, M0 (according to the staging of 7th edition of Union for International Cancer Control)¹

Primary pancreatic surgery was performed within 12 weeks before the start of study treatment

No distant metastatic disease, or local disease was confirmed by imaging within 14 days before registration in the clinical trial

Eastern Cooperative Oncology Group performance status is 0 or 1

Data within 7 days before enrollment meet the following criteria for bone marrow, liver, kidney, and metabolic function:

- Neutrophil count[†] more than 1500/mm³
- Hemoglobin[‡] ≥9.0 g/dL
- Platelet count[§] ≥100,000/mm³
- Total bilirubin below the upper limit of normal (ULN) according to the standard assay used at the trial site
- Aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase no more than 2.5 times the ULN according to the standard assay used at the trial site
- Creatinine clearance (CLcr)^{||} ≥ 50 mL/min or more
- Glycosylated hemoglobin (HbA1c)[¶] ≤8.4% (using National Glycohemoglobin Standardization Program testing criteria)

CA19-9 <100 U/mL based on tests performed within 14 days prior to enrollment

*Give priority to the overall findings.

[†]Excluding measurements within 7 days after administration of granulocyte colony-stimulating factor.

[‡]Excluding measurements within 28 days of transfusion.

[§]Excluding measurements within 7 days after platelet transfusion.

^{||}If urine collection was performed, the value should be used. If there are no observed values, the following Cockcroft-Gault Estimates are used for the estimation:

CLcr estimate = [(140-age) × body weight]/ [72 × serum creatinine] (for women, multiply the obtained value by 0.85).

[¶]Tested up to 14 days before enrollment.

SUPPLEMENTARY TABLE 2. Complete Exclusion Criteria

- Patients who have received prior treatment other than surgery for primary pancreatic cancer (chemotherapy, radiotherapy, etc.)
- A history of pancreatic cancer with distant metastatic disease
- A history of concurrent active cancer or metachronous cancer within 5 years; however, lesions equivalent to carcinoma in situ or upper mucosal carcinoma that was determined, by the investigators, to be cured by local treatment are not included in the history of cancer
- Severe drug hypersensitivity
- Concomitant use of immunosuppressive drugs or biological response modulators that may suppress bone marrow
- Active infections that require systemic treatment (confirmed by the presence of infection-related pyrexia of $\geq 38^{\circ}\text{C}$, increased C-reactive protein level, etc.)
- A risk of bleeding defined by the presence of increased bleeding time (exceeding standard value +15% of prothrombin time, partial prothrombin time, etc.) or the use of warfarin
- Participation in clinical trials or studies that affect the evaluation of this study
- Current or past history of the following diseases:
- Myocardial infarction, severe unstable angina, coronary/peripheral vascular bypass graft, symptomatic congestive heart failure (New York Heart Association class III–IV), uncontrolled hypertension, clinically significant cardiac rhythm abnormalities or electrocardiogram abnormalities, cerebrovascular accident, transient ischemic attack or seizure disorder within 24 weeks prior to enrollment
 - Postoperative complications such as intra-abdominal bleeding, portal vein thrombosis, splenic pseudoaneurysm, bile duct anastomotic leak, gastrointestinal bleeding, deep vein thrombosis or pulmonary embolism
 - Serious collagen diseases (lupus nephritis, scleroderma, arteritis nodosa, etc.)
 - Interstitial lung disease, slowly progressive dyspnea and dry cough, silicosis, idiopathic pulmonary fibrosis or pulmonary hypersensitivity pneumonitis
 - Human immunodeficiency virus infection, diseases related to acquired immunodeficiency syndrome, or active hepatitis (patients with positive hepatitis B virus surface antigen or hepatitis C virus [HCV] antibody); patients with positive HCV antibody but with negative HCV-RNA can be enrolled
 - Poorly controlled diabetes mellitus or severe diabetes mellitus (eg, those with advanced diabetic complications)
- Grade ≥ 2 peripheral sensory or motor neuropathy
- Receipt of continuous systemic steroids (oral or intravenous)
- Mental disorder or psychiatric symptoms that, in the opinion of the investigator, would make it difficult for the patient to participate in the clinical trial
- Pregnancy or lactation,* or unwillingness to use contraception for 180 days during the study period and after the last dose of the investigational product, etc. Women of childbearing potential[†] should be interviewed and pregnancy tests performed prior to enrollment
- The investigator considered the patient to be an inappropriate candidate for the study
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*Subjects who discontinue breastfeeding are not allowed to participate in the study.

[†]Women of childbearing potential means that there is a medical rationale for considering the patient to be capable of falling pregnant, such as premenopausal woman, women who have not had a menstrual period for <1 year after the prior menstrual period or for >1 year for medical reasons such as drug administration, and women without permanent contraception.

Reference

1. International Union Against Cancer (UICC). *TNM Classification of Malignant Tumours, 7th Edition*. Hoboken, NJ: Wiley-Blackwell; 2011.