Supplementary

Appendix 1 Inclusion and exclusion criteria

Inclusion criteria

For inclusion in this study, subjects were required to fulfil the following criteria:

(I) Age >20 years
(II) Histologically confirmed adenocarcinoma by WHO classification
(III) Pathologic stage IB-IIIA
(IV) Completely resected primary tumor after surgery (R0 resection) before participating this study. R0 resection is defined as follows:
  i. N1-2: R0 resection with lobectomy and mediastinal lymph node dissection (MLND)
  ii. N0: R0 resection with lobectomy with or without MLND
(V) Less than 10% of body weight loss 3 months ago
(VI) Normal function of the main organs:
  i. WBC: >3,000/mm^3 (Neutrophil count: >1,500/mm^3)
  ii. Hemoglobin: >9.0 g/dL
  iii. Platelet count: >100,000/mm^3
  iv. Both AST and ALT: <2.5× UNL
  v. Total bilirubin: ≤1.5× ULN
  vi. Serum creatinine: ≤1.5 mg/dL
  vii. Creatinine clearance: >30 mL/min (actual measurement or the value obtained using the Cockcroft-Gault formula)
(VII) Absence of hematological toxicity or hormonal therapy
(VIII) Provision of informed consent prior to any study-specific procedures
(IX) Performance status (ECOG) of 0 or 1.
(X) Willingness and ability to comply with the protocol for the duration of the study, including undergoing treatment and scheduled visits and examinations, including follow-up
(XI) Females must be taking medically approved contraceptive measures (condom, infertility surgery, oral contraceptives, etc.) during the treatment, and must have a negative urine stick or blood pregnancy test result 21 days prior to the start of dosing, if of child-bearing potential or must have evidence of non-child-bearing potential by fulfilling one of the following criteria at screening: (i) post-menopausal, defined as aged more than 50 years and amenorrhoeic for at least 12 months following cessation of all exogenous hormonal treatments, (ii) women under 50 years of age were considered postmenopausal if they had been amenorrhoeic for 12 months or more following cessation of exogenous hormonal treatments and with luteinizing hormone and follicle-stimulating hormone levels in the post-menopausal range for the institution; (iii) documentation of irreversible surgical sterilization by hysterectomy, bilateral oophorectomy, or bilateral salpingectomy, but not tubal ligation.

Exclusion criteria

Subjects did not enter the study if any of the following exclusion criteria were fulfilled:

(I) Presence of active double cancer (synchronous double cancer and metachronous double cancer within a 5-year disease-free interval are defined as active double cancer)
(II) Previously treated with preoperative chemotherapy
(III) The need for postoperative radiation therapy
(IV) Distant metastasis except regional lymph node metastasis
(V) Less than 2 weeks after serious infections requiring antibiotics administration
(VI) Positive for HIV infection
(VII) Serious cardiopulmonary dysfunction by investigator assessment

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(VIII) Women who will not be compliant with a medically approved contraceptive regimen during the treatment period or lactating women.

(IX) History of autoimmune disorder or current treatment with immunotherapy

(X) Symptomatic neuropathy > CTC grade 1

(XI) Any evidence of severe disease or medical condition, which in the investigator's opinion make it undesirable for the patient to participate in the trial or would jeopardize compliance with the protocol, including uncontrolled hypertension, coronary artery disease, diabetes, metabolic syndrome or other serious systemic illness.

(XII) Judgment by the investigator that the patient should not participate in the study if the patient is unlikely to comply with study procedures, restrictions, and requirements

(XIII) Any evidence of active bleeding diatheses, regardless of cancer

(XIV) Participation in other clinical trials after registration in this trial, or having participated in other clinical trials within 3 months before registration in this trial

(XV) Others judged by the investigator to be unsuitable for the study

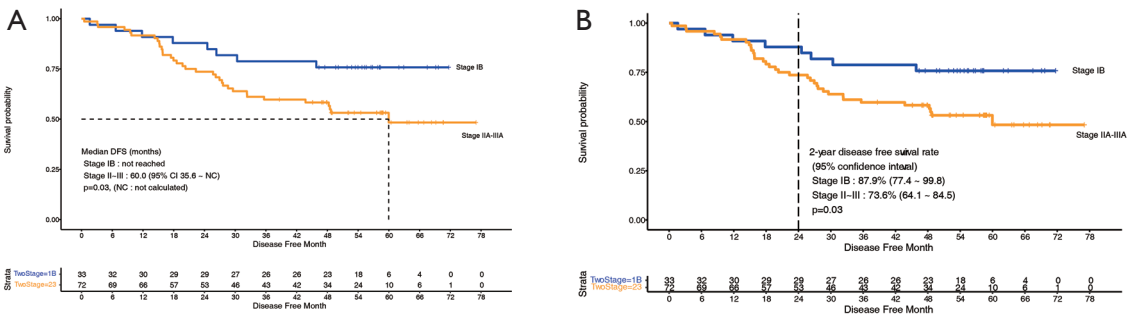

Figure S1 Kaplan-Meier curves for DFS. Stage IB versus IIA–IIIA disease (A), and 2-year DFSR in stage IB versus IIA–IIIA disease (B). DFS, disease-free survival; DFSR, disease-free survival rate.

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Table S1 Adverse events that occurred in the safety population (n=105)

Adverse events	No. of patients (%)			
	All Grades	Grade 1	Grade 2	Grade 3
Any adverse events	101 (96.2)	101 (96.2)	48 (45.7)	10 (9.5)
Hematologic adverse events				
White blood cell decreased	16 (15.2)	6 (5.7)	7 (6.7	3 (2.9)
Anemia	5 (4.8)	3 (2.9)	2 (1.9)	0 (0.0)
Platelet count decreased	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Leukocytosis	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Non-hematologic adverse events				
Nausea	63 (60.0)	41 (39.0)	22 (21.0)	1 (1.0)
Anorexia	47 (44.8)	45 (42.9)	3 (2.9)	0 (0.0)
Cough	41 (39.0)	41 (39.0)	1 (1.0)	0 (0.0)
Fatigue	41 (39.0)	39 (37.1)	3 (2.9)	0 (0.0)
Constipation	28 (26.7)	26 (24.8)	3 (2.9)	0 (0.0)
Vomiting	28 (26.7)	20 (19.0)	8 (7.6)	1 (1.0)
Abdominal pain	20 (19.0)	19 (18.1)	1 (1.0)	0 (0.0)
Diarrhea	18 (17.1)	18 (17.1)	1 (1.0)	0 (0.0)
Insomnia	18 (17.1)	17 (16.2)	1 (1.0)	0 (0.0)
Dyspnea	16 (15.2)	13 (12.4)	4 (3.8)	0 (0.0)
Productive cough	16 (15.2)	14 (13.3)	2 (1.9)	0 (0.0)
Dizziness	12 (11.4)	12 (11.4)	0 (0.0)	0 (0.0)
Upper respiratory infection	12 (11.4)	12 (11.4)	0 (0.0)	0 (0.0)
Myalgia	10 (9.5)	8 (7.6)	2 (1.9)	0 (0.0)
Dyspepsia	9 (8.6)	8 (7.6)	1 (1.0)	0 (0.0)
Liver enzyme increased	9 (8.6)	6 (5.7)	2 (1.9)	1 (1.0)
Pruritus	9 (8.6)	8 (7.6)	1 (1.0)	0 (0.0)
Hiccups	8 (7.6)	8 (7.6)	0 (0.0)	0 (0.0)
Mucositis oral	8 (7.6)	8 (7.6)	0 (0.0)	0 (0.0)
Paresthesia	8 (7.6)	8 (7.6)	0 (0.0)	0 (0.0)
Allergic rhinitis	7 (6.7)	7 (6.7)	0 (0.0)	0 (0.0)
Headache	7 (6.7)	6 (5.7)	1 (1.0)	0 (0.0)
Back pain	6 (5.7)	4 (3.8)	2 (1.9)	0 (0.0)
Rash maculo-papular	6 (5.7)	6 (5.7)	0 (0.0)	0 (0.0)
Sore throat	6 (5.7)	5 (4.8)	1 (1.0)	0 (0.0)
Edema limbs	5 (4.8)	5 (4.8)	0 (0.0)	0 (0.0)
Fever	5 (4.8)	3 (2.9)	2 (1.9)	0 (0.0)
Hyperglycemia	5 (4.8)	3 (2.9)	1 (1.0)	1 (1.0)
Lung infection	5 (4.8)	2 (1.9)	3 (2.9)	0 (0.0)
Pain in extremity	5 (4.8)	3 (2.9)	2 (1.9)	0 (0.0)
Skin infection	5 (4.8)	5 (4.8)	0 (0.0)	0 (0.0)
Alopecia	4 (3.8)	4 (3.8)	0 (0.0)	0 (0.0)
Gastroesophageal reflux disease	4 (3.8)	3 (2.9)	1 (1.0)	0 (0.0)
Peripheral sensory neuropathy	4 (3.8)	4 (3.8)	0 (0.0)	0 (0.0)
Urticaria	4 (3.8)	3 (2.9)	1 (1.0)	0 (0.0)
Acute kidney injury	3 (2.9)	2 (1.9)	1 (1.0)	0 (0.0)
Arthralgia	3 (2.9)	2 (1.9)	1 (1.0)	0 (0.0)
Bloating	3 (2.9)	3 (2.9)	0 (0.0)	0 (0.0)
Chest pain - cardiac	3 (2.9)	3 (2.9)	0 (0.0)	0 (0.0)
Cystitis	3 (2.9)	3 (2.9)	0 (0.0)	0 (0.0)
Gastritis	3 (2.9)	2 (1.9)	1 (1.0)	0 (0.0)
Thromboembolic event	3 (2.9)	0 (0.0)	0 (0.0)	3 (2.9)
Hoarseness	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Hyperhidrosis	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Hypokalemia	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Hypomagnesemia	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Neoplasms	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Non-cardiac chest pain	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Pharyngitis	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Pleuritic pain	2 (1.9)	1 (1.0)	1 (1.0)	0 (0.0)
Tremor	2 (1.9)	2 (1.9)	0 (0.0)	0 (0.0)
Acute coronary syndrome	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Anxiety	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Blurred vision	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Colitis	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Dry mouth	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Edema face	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Esophageal infection	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Eyelid function disorder	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Facial nerve disorder	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Facial pain	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Hearing impaired	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Hematuria	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Hemorrhoids	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Hypertension	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Hypocalcemia	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Hyponatremia	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Hypothyroidism	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Irregular menstruation	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Malaise	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Mucosal infection	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Neuralgia	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Otitis media	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Pancreatitis	1 (1.0)	0 (0.0)	0 (0.0)	1 (1.0)
Pleural effusion	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Pneumothorax	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Proteinuria	1 (1.0)	0 (0.0)	1 (1.0)	0 (0.0)
Sinus tachycardia	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Skin hyperpigmentation	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Upper gastrointestinal hemorrhage	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Urinary frequency	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Urinary incontinence	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Urinary tract pain	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Vaginal infection	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)
Bronchial infection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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Table S2 Adverse events that occurred in the safety population (all events)

Adverse events	No. of events (%)			
	All Grades	Grade 1	Grade 2	Grade 3
Any adverse events	603	500	92	11
Hematologic adverse events				
Anemia	5 (0.8)	3 (0.6)	2 (2.2)	0 (0.0)
Leukocytosis	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Platelet count decreased	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
White blood cell decreased	16 (2.7)	6 (1.2)	7 (7.6)	3 (27.3)
Non-hematologic adverse events				
Abdominal pain	20 (3.3)	19 (3.8)	1 (1.1)	0 (0.0)
Acute coronary syndrome	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Acute kidney injury	3 (0.5)	2 (0.4)	1 (1.1)	0 (0.0)
Allergic rhinitis	7 (1.2)	7 (1.4)	0 (0)	0 (0.0)
Alopecia	4 (0.7)	4 (0.8)	0 (0)	0 (0.0)
Anorexia	47 (7.8)	45 (9)	3 (3.3)	0 (0.0)
Anxiety	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Arthralgia	3 (0.5)	2 (0.4)	1 (1.1)	0 (0.0)
Back pain	6 (1.0)	4 (0.8)	2 (2.2)	0 (0.0)
Bloating	3 (0.5)	3 (0.6)	0 (0)	0 (0.0)
Blurred vision	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Chest pain - cardiac	3 (0.5)	3 (0.6)	0 (0)	0 (0.0)
Colitis	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Constipation	28 (4.6)	26 (5.2)	3 (3.3)	0 (0.0)
Cough	41 (6.8)	41 (8.2)	1 (1.1)	0 (0.0)
Cystitis	3 (0.5)	3 (0.6)	0 (0)	0 (0.0)
Diarrhea	18 (3.0)	18 (3.6)	1 (1.1)	0 (0.0)
Dizziness	12 (2.0)	12 (2.4)	0 (0)	0 (0.0)
Dry mouth	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Dyspepsia	9 (1.5)	8 (1.6)	1 (1.1)	0 (0.0)
Dyspnea	16 (2.7)	13 (2.6)	4 (4.3)	0 (0.0)
Edema face	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Edema limbs	5 (0.8)	5 (1)	0 (0)	0 (0.0)
Esophageal infection	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Eyelid function disorder	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Facial nerve disorder	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Facial pain	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Fatigue	41 (6.8)	39 (7.8)	3 (3.3)	0 (0.0)
Fever	5 (0.8)	3 (0.6)	2 (2.2)	0 (0.0)
Gastritis	3 (0.5)	2 (0.4)	1 (1.1)	0 (0.0)
Gastroesophageal reflux disease	4 (0.7)	3 (0.6)	1 (1.1)	0 (0.0)
Headache	7 (1.2)	6 (1.2)	1 (1.1)	0 (0.0)
Hearing impaired	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Hematuria	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Hemorrhoids	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Hiccups	8 (1.3)	8 (1.6)	0 (0)	0 (0.0)
Hoarseness	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
Hyperglycemia	5 (0.8)	3 (0.6)	1 (1.1)	1 (9.1)
Hyperhidrosis	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
Hypertension	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Hypocalcemia	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Hypokalemia	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
Hypomagnesemia	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
Hyponatremia	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Hypothyroidism	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Insomnia	18 (3.0)	17 (3.4)	1 (1.1)	0 (0.0)
Irregular menstruation	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Liver enzyme increased	9 (1.5)	6 (1.2)	2 (2.2)	1 (9.1)
Lung infection	5 (0.8)	2 (0.4)	3 (3.3)	0 (0.0)
Malaise	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Mucosal infection	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Mucositis oral	8 (1.3)	8 (1.6)	0 (0)	0 (0.0)
Myalgia	10 (1.7)	8 (1.6)	2 (2.2)	0 (0.0)
Nausea	63 (10.4)	41 (8.2)	22 (23.9)	1 (9.1)
Neoplasms	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
Neuralgia	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Non-cardiac chest pain	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
Otitis media	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Pain in extremity	5 (0.8)	3 (0.6)	2 (2.2)	0 (0.0)
Pancreatitis	1 (0.2)	0 (0)	0 (0)	1 (9.1)
Paresthesia	8 (1.3)	8 (1.6)	0 (0)	0 (0.0)
Peripheral sensory neuropathy	4 (0.7)	4 (0.8)	0 (0)	0 (0.0)
Pharyngitis	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
Pleural effusion	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Pleuritic pain	2 (0.3)	1 (0.2)	1 (1.1)	0 (0.0)
Pneumothorax	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Productive cough	16 (2.7)	14 (2.8)	2 (2.2)	0 (0.0)
Proteinuria	1 (0.2)	0 (0)	1 (1.1)	0 (0.0)
Pruritus	9 (1.5)	8 (1.6)	1 (1.1)	0 (0.0)
Rash maculo-papular	6 (1.0)	6 (1.2)	0 (0)	0 (0.0)
Sinus tachycardia	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Skin hyperpigmentation	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Skin infection	5 (0.8)	5 (1)	0 (0)	0 (0.0)
Sore throat	6 (1.0)	5 (1)	1 (1.1)	0 (0.0)
Thromboembolic event	3 (0.5)	0 (0)	0 (0)	3 (27.3)
Tremor	2 (0.3)	2 (0.4)	0 (0)	0 (0.0)
Upper gastrointestinal hemorrhage	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Upper respiratory infection	12 (2.0)	12 (2.4)	0 (0)	0 (0.0)
Urinary frequency	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Urinary incontinence	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Urinary tract pain	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Urticaria	4 (0.7)	3 (0.6)	1 (1.1)	0 (0.0)
Vaginal infection	1 (0.2)	1 (0.2)	0 (0)	0 (0.0)
Vomiting	28 (4.6)	20 (4)	8 (8.7)	1 (9.1)

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