

A Single-Arm, Single-Center, Phase II Study of AK104 Plus Chemotherapy as Neoadjuvant/Adjuvant Therapy for Resectable PD-L1-Negative NSCLC (Stage IB [≥4cm]–IIIB [N2])

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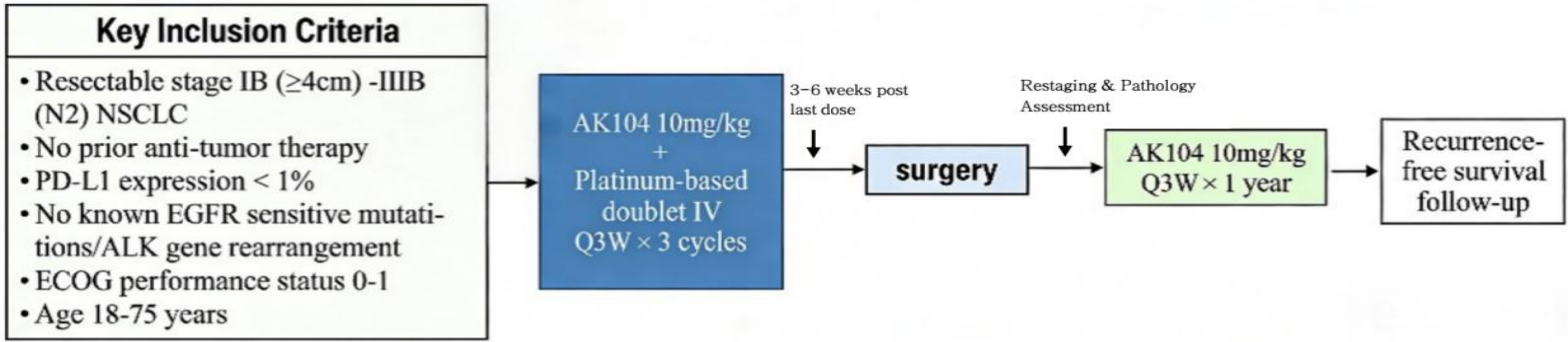
Background

Perioperative PD-1-based chemo-immunotherapy is standard for resectable NSCLC, with limited benefit for PD-L1-negative disease. AK104 (PD-1/CTLA-4 bispecific antibody) shows promising activity in advanced PD-L1-negative NSCLC. This phase II study evaluates AK104-chemotherapy in PD-L1-negative resectable NSCLC (IB ≥4 cm-IIIB N2), targeting unmet perioperative treatment needs in Chinese patients.

Study Objectives

- Primary endpoint:
- Major pathological response (MPR), defined as ≤10% residual viable tumor cells in the tumor bed.
- Secondary endpoints:
- pCR : No invasive or in-situ residual tumor in lung tissues and lymph nodes.
 - ORR : Confirmed CR or PR according to RECIST 1.1.
 - EFS24: Event-free survival at 24 months after diagnosis.
 - TEAEs : All adverse events occurring during treatment, evaluated for type, frequency and severity.

Study Design



Patients received 3 cycles of neoadjuvant therapy: AK104 10 mg/kg (d1, q3w) plus either paclitaxel 175 mg/m or albumin-bound paclitaxel 260 mg/m (>30 min infusion, d1, q3w), combined with carboplatin at AUC 5 (d1, q3w). Surgical resection was performed 3–6 weeks after neoadjuvant completion. Postoperatively, patients received up to 12 months of adjuvant therapy.

Eligibility criteria

- Inclusion**
 - Age 18–70 years
 - Resectable NSCLC, stage IB (≥4 cm)–IIIB (N2)
 - EGFR/ALK/ROS1 wild-type, PD-L1 TPS < 1%
 - ECOG 0–1
 - Treatment-naïve
 - Measurable lesions (RECIST 1.1) with available baseline tumor tissue
 - Adequate major organ function
- Exclusion**
 - Mixed histology or small cell components, unresectable/metastatic disease
 - Tumor with high bleeding/necrosis/vascular invasion risk
 - Prior systemic anticancer therapy or thoracic radiotherapy
 - Malignancy history within 5 years (except cured superficial tumors)
 - Allergy to cadonilimab or chemotherapy components
 - Active interstitial lung disease, uncontrolled severe diseases
 - Cerebrovascular events or pulmonary embolism within 6 months
 - ≥Grade 2 peripheral neuropathy, recent major surgery within 14 days
 - Concurrent clinical trial participation
 - Severe antibody hypersensitivity history
 - Pregnancy/lactation, uncontrolled neurological or psychiatric disorder

Study Status

- Clinical trial identification: NCT06532591
- Ethics approval has been obtained. Enrollment is in progress.
- Planned enrollment: 20 patients.
- First-in-patient dosed: October 30, 2024
- Enrollment status: 9 patients have been enrolled

Anticipated Outcomes

- Expected higher MPR in PD-L1-negative resectable NSCLC
- Manageable safety profile

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