ALTER-L003: Anlotinib Hydrochloride Combined With AP in Stage IIIB/IIIC/IV Non-squamous Non-small-cell Lung Cancer

NCT number: NCT04012619

Date: 2018.07.01

Version：1.0

Study population

Eligible patients had histologically or cytologically con frmed stage IIIB/IIIC/IV nonsquamous NSCLC; were nega tive for mutations of EGFR\ALK\ROS1; were aged 18 to 70; never received any systematic treatment (including immu notherapy); had an Eastern Cooperative Oncology Group (ECOG) performance status 0 – 1; had an expected survival time ⩾ 3 months; and presented no major organ dysfunction. Patients were excluded if they had active brain metastases, uncontrolled hypertension, severe cardiovascular diseases, or coagulation abnormalities. This study was reviewed and approved by the Institutional Review Board of West China Hospital, Sichuan University. Written informed consent was obtained from all participants.

This study is registered with ClinicalTrials.gov, number NCT04012619.

Study design

This study employed a standard 3+3 dose reduction design and eligible patients received anlotinib-chemotherapy regimen on 21-day cycles for 4 cycles. Pemetrexed (500 mg/m^2) and cisplatin (75 mg/m^2) or carboplatin (AUC = 5) were intravenously given on day 1 of each cycle. According to the ALTER0303 study, the initial dose of anlotinib was set as 12 mg/day with a 2-week on/1-week off schedule, and was reduced to 10 mg/day and 8 mg/day in sequence depending on DLTs in cycle 1. Patients who had disease control after the combination regimen continued to receive anlotinib maintenance until disease progression.

Assessments

The primary endpoint was the MTD of anlotinib, at which less than 33% of patients experienced a DLT in the first treatment cycle. DLT was defined as grade 4 and above hematological toxicity, grade 2 and above liver and kidney function injury and grade 3 and above non-hematological toxicity. The secondary endpoints included PFS and OS. PFS was defined as the time from the date of randomization to the date of disease progression or death. OS was defined as the time from the date of randomization to the date of death.

Statistical analysis

Recruitment of a minimum of 3 patients and a maximum of 18 patients was planned in accordance with the 3+3 study design. All patients who received at least one dose of the investigational drug were included in safety assessment and those who completed at least one cycle of the treatment were eligible for efficacy evaluation. The baseline demographic characteristics and frequency of adverse events were summarised with descriptive statistics. Two-sided 95% exact CIs were calculated for ORR and DCR using the Clopper-Pearson method, and estimated time-to-event endpoints were calculated with the Kaplan-Meier method with two-sided 95% CIs for medians. All statistical analyses were carried out with SAS 9.1.3 software.