A phase II, Prospective, Randomized, open label, multi-center study of Tislelizumab combined with Anlotinib and Platinum Doublet Chemotherapy as Neoadjuvant/Adjuvant with Resectable Stage II-IIIB Non-Small Cell Lung Cancer

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Applicant: Tangdu Hospital, Air Force Military Medical University

Main researcher: Professor Yan Xiaolong

Brief summary:

This is a Phase II, prospective, randomized, open label, controlled, multi-center study, aim to evaluate the activity of Tislelizumab and Anlotinib and chemotherapy compared with Tislelizumab and chemotherapy before surgery, followed by Tislelizumab alone as adjuvant therapy. in terms of pathological complete response. The primary objective of this study is to evaluate and compare pathological complete response rate(pCR).

Study Type : Interventional (Clinical Trial)

Actual Enrollment : 178 participants

Allocation: Randomized

Intervention Model: Parallel Assignment

Masking: open label

Primary Purpose: Treatment

Official Title: A phase II, Prospective, Randomized, open label, multi-center study of Tislelizumab combined with Anlotinib and Platinum Doublet Chemotherapy as Neoadjuvant/Adjuvant with Resectable Stage II-IIIB Non-Small Cell Lung Cancer

Arms and Interventions

Experimental A: Experimental Group: Tislelizumab with anlotinib and platinum-based chemotherapy + Adjuvant Tislelizumab (n=89)

Intervention/treatment:

Tislelizumab 200mg iv, d1, q3w,

Anlotinib 10mg, po, qd1-14, q3w,

Cisplatin 75 mg/m^2 by IV infusion Q3W, given on cycle day 1

Carboplatin AUC of 5 on Day 1 of each 3-week cycle

Paclitaxel 175mg/m2 on Day 1 of each 3-week cycle(SQ only)

Albumin-bound paclitaxel 260mg/m2, on D1 IV infusion Q3W or 130mg/m2 on D1D8 IV infusion Q3W for each cycle(SQ only)

Pemetrexed 500 mg/m2 on Day 1 of each 3-week cycle(NSQ only)

Adjuvant: 4 weeks(±7 Days) following surgery, participants receive no more than 16 cycles (cycle length: 3 weeks) of Tislelizumab [200 mg, IV; given on cycle day 1].

Active Comparator B: Control group: Tislelizumab with platinum-based chemotherapy + Adjuvant Tislelizumab (n=89)

Intervention/treatment:

Tislelizumab 200mg iv, d1, q3w,

Cisplatin 75 mg/m^2 by IV infusion Q3W, given on cycle day 1

Carboplatin AUC of 5 on Day 1 of each 3-week cycle

Paclitaxel 175mg/m2 on Day 1 of each 3-week cycle(SQ only)

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Outcome Measures

Primary Outcome Measures

pathological complete response (pCR) in Intent-to-Treat (ITT) analysis set

no residual tumor cells in the surgically resected tumor specimen and all sampled regional lymph nodes after neoadjuvant treatment.

Secondary Outcome Measures

main pathology rate (MPR) in ITT analysis set

Major pathological response rate (MPR): defined as ⩽ 10% of residual tumor cells in the surgically resected tumor specimen and sampled regional lymph nodes after neoadjuvant treatment.

Event-free survival (EFS) in ITT analysis set: defined as the time from the randomization until the date of first documented RESCIST 1.1 disease progression or local or distant recurrence of lung cancer or date of death due to any cause, whichever came first.

Objective Response Rate (ORR) in ITT analysis set

defined as the proportion of participants with complete response (CR) and partial response (PR), as assessed by the RECIST v1.1

Overall Survival (OS)

defined as the time from randomization until the date of death due to any cause

Adverse Events (AEs)

The number of participants experiencing an AE will be assessed by CTCAE v5.0.

Other Outcome Measures:

Biomarker, R0 resection rate, type of surgery

Eligibility Criteria

Ages Eligible for Study: 18 Years and older (Adult, Older Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: No

Criteria

Key Inclusion Criteria:

1. aged 18~75 years old
2. histologically confirmed stage IIA to stage IIIB (IIIB term T2/3/4N2) non-small cell lung cancer (staging based on AJCC 9th edition)
3. ECOG PS score of 0-1;
4. patients are asked to provide an archived tumor tissue sample (FFPE tissue block or approximately ⩾ 6 freshly cut unstained FFPE sections) and a pathology report of this baseline sample for PD-L1 and other biomarker analysis). Biopsy samples are requested at baseline if there are no available archival samples or samples are unavailable.
5. Adequate organ and marrow function
6. expected survival ⩾ 3 months;
7. be evaluated by a thoracic surgeon and confirmed to be eligible for R0 resection for the purpose of radical treatment
8. At least 1 lesion, not previously irradiated, that qualifies as a RECIST 1.1 Target Lesion (TL) at baseline

Key Exclusion Criteria:

1. those with a known history of CNS metastases;
2. patients with EGFR mutations or ALK translocations;
3. those with imaging (CT or MRI) showing tumor invasion of a major blood vessel (e.g., pulmonary artery or superior vena cava) or those with a high likelihood of fatal

hemorrhage due to tumor invasion of a major blood vessel during the follow-up study;

4. prior treatment with immune checkpoint inhibitors, including but not limited to anti-CTLA-4, anti-PD-1 and anti-PD-L1 therapeutic antibodies, and OX-40;
5. previous systemic antivascular therapy;
6. current participation in an interventional clinical trial or receipt of another investigational drug or medical intervention within 4 weeks;
7. presence of active hemoptysis, active diverticulitis, abdominal abscess, gastrointestinal obstruction (or other factors affecting the absorption of oral medications such as inability to swallow, nausea and vomiting, abnormal physiologic function, malabsorption syndrome, etc.) that require clinical intervention
8. the presence of any signs or history of bleeding constitution; the presence of unhealed wounds, ulcers, or fractures in patients who have experienced any bleeding or hemorrhagic event ⩾ CTCAE Grade 3 within 4 weeks prior to enrollment;
9. class III-IV congestive heart failure with poorly controlled and clinically significant arrhythmias (including QTcF ⩾450ms in men and ⩾470ms in women);
10. difficult-to-control hypertension;
11. history of severe allergy to amlotinib or its prophylactic agents;
12. any arterial thrombosis, embolism, or ischemia, such as myocardial infarction, unstable angina, cerebrovascular accident, or transient cerebral ischemic attack, that has occurred within 6 months prior to enrollment in therapy
13. patients whose medical history or test results indicate a hereditary predisposition to bleeding or coagulation disorders that may increase the risk of bleeding
14. active autoimmune disease requiring systemic treatment or history of autoimmune disease with potential for relapse
15. patients requiring long-term systemic glucocorticosteroids (patients requiring inhaled or locally injected glucocorticosteroids due to COPD, asthma may be enrolled) or who have received immunosuppressive therapy within 7 days prior to treatment
16. have an active infection requiring treatment or have used systemic anti-infective medications within one week prior to the first dose;
17. a history of interstitial lung disease, non-infectious pneumonia, or poorly controlled disease, including pulmonary fibrosis, acute lung disease
18. a known history of human immunodeficiency virus (HIV) infection, untreated active hepatitis B (defined as HBsAg positivity along with a detectable HBV-DNA copy number greater than 2,000 IU/ml, and active HCV-infected subjects (HCV antibody positivity with HCV-RNA levels above the lower limit of detection);
19. previous allogeneic stem cell transplantation or organ transplantation.
20. have received a live vaccine within 30 days prior to the first dose (Cycle 1, Day 1);
21. pregnant or lactating women;
22. patients with hypersensitivity to the study drug or excipients;
23. history or evidence of disease that may interfere with the results of the trial, prevent the subject from participating in the study in its entirety, abnormal values of therapeutic or laboratory tests, or other conditions that, in the opinion of the investigator, make enrollment inappropriate The investigator believes that there are other potential risks that make participation in the study inappropriate;

24. stage IIIB exclusion of patients with TxN3 non-small cell lung cancer (staging based on AJCC 9th edition);
25. renal insufficiency: routine urinalysis suggestive of urinary protein ⩾++ or confirmed 24-hour urinary protein volume ⩾1.0 g;
26. patients with central squamous cell carcinoma confirmed by imaging and pathology;

Locations

China, Shannxi

The Second Affiliated Hospital of Air Force Medical University

Xi'an, Shannxi, China

Sponsors and Collaborators

Tang-Du Hospital

Investigators

Principal Investigator: Xiaolong Yan, PhD