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Liquid tumor-infiltrating lymphocytes (L-TIL) plus tislelizumab and chemotherapy for stage IV non-small cell lung cancer patients who failed from prior anti-PD-1 antibody combined with chemotherapy

-Single-arm, single-center, phase II clinical study

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Objectives

1. Primary endpoint

Investigator assessed Objective Response Rate (ORR) by RECIST V1.1

2. Secondary endpoints

Investigator assessed Progression Free Survival (PFS) according to RECIST V1.1

Investigator assessed Disease Control Rate (DCR) according to RECIST V1.1;

Investigator assessed Duration of Response (DOR) according to RECIST V1.1;

One-year and two-year's overall survival rate;

Safety and adverse events of L-TIL in combination with tislelizumab and chemotherapy, including the incidence of adverse events (AEs), serious adverse events (SAEs), and the incidence rate of treatment discontinuation due to AEs/SAEs.

3. Exploratory endpoint

Assessment of the distribution characteristics of the subject's immune cell subsets

Study design

This study is a single-arm, single-center, phase II clinical study. For patients who failed from previous anti-PD-1 antibody plus chemotherapy, the subjects are eligible for enrollment. Induction treatment comprised four 21-day cycles of liquid tumor infiltrating lymphocyte therapy (3-10)x10^9/m^2 intravenously on day14 (Q3W), combined with Tislelizumab 200 mg intravenously on day 1 (Q3W) and Docetaxel (75mg/m^2, day 1 of each 21-day cycle). After that, non-PD responders will continue to receive 2 cycles of L-TIL and one year of Tislelizumab maintenance therapy.

Statistical Analysis Plan

For the second-line treatment of advanced non-small cell lung cancer, previous Phase II/III clinical studies including Checkmate-017 (n=272), Checkmate-057 (n=582), Keynote-010 (n=1033), OAK (n=850), Checkmate-078 (n=504), ORIENT-03 (n=290) and RATIONALE-303 (n=805) showed the ORR of Docetaxel and single PD-1 inhibitor were 2.2-13% and 14-25.5%, respectively. No data is available about the ORR of subsequent PD-1 inhibitors for the patients who have failed from previous anti-PD-1 based therapy. In order to preliminarily evaluate the efficacy and safety of L-TIL plus tislelizumab and Docetaxel, a two-stage design model of Simon was adopted, with a hypothesis of objective response rate (ORR0) ≤10% and ORR1≥30%. The probability of Class I error is 0.05 and the Class II error is 0.10. Based on these previous parameters, the first phase of enrollment needs 18 patients. Once 2 patients achieve partial response, the study entered into the second phage and fifteen more subjects will be needed. If six partial response occur in the total of 33 enrolled subjects, the trial will achieve primary endpoint and be successful.