PHASE II CLINICAL STUDY OF TORIPALIMAB IN COMBINATION WITH STEREOTACTIC RADIOTHERAPY AS A NEOADJUVANT THERAPY FOR THE TREATMENT OF RESECTABLE (N1-N2) NON-SMALL CELL LUNG CANCER

Zhen Wang*, Xi-xu Zhu, Yong Song. Nanjing Jinling Hospital, Nanjing, China

Background Background: Early stage non-small cell lung cancer (NSCLC) possessed highly local and distant recurrence rates after surgery. Recent studies showed neoadjuvant therapy can improve pathological response and postoperative survival.¹⁻³ Using immune checkpoint inhibitors as a neoadjuvant treatment could release neoantigens from dying tumour cells and stimulate the priming and expansion of neoantigen-specific T cells in the tumour before surgical resection.⁴ Previous study indicated radiotherapy combined with chemotherapy as neoadjuvant didn't improve event-free or overall survival in stage III/N2 NSCLC.⁵ Subsequently, the study of neoadjuvant chemoradiation plus pembrolizumab have demonstrated that radiotherapy can enhance the effect of immunotherapy, achieving better complete pathological response.⁶ Stereotactic body radiation therapy (SBRT) is a precise radiotherapy model that has shown good efficacy in treating early lung cancer, combining with immunotherapy as neoadjuvant therapy for NSCLC may improve pathological response and postoperative survival.

Methods This is a prospective, single-center, two-part, phase II study assessing the safety, tolerability and efficacy of SBRT combined with toripalimab as neoadjuvant in patients with stage IIB–IIIA NSCLC without driver mutations (Clinical trial information: ChiCTR2000029277). Eligibility criteria include IIB–IIIA NSCLC (AJCC v8), adequate organ function, and ECOG PS 0 or 1. The primary endpoints were the safety and pathologic response, while the secondary endpoint was the radiographic response, recurrence-free survival and overall survival. The trial also aimed at exploring prognosis biomarkers (included Tumor infiltrates lymphocytes, CD8+Tcell, PD-L1 protein expression, tTMB and the correlation with pathologic response rate). 30 patients will receive SBRT (50 Gy/5 fractions over 5 days) on the first week. Afterwards, all patients will receive 2 cycles of intravenous toripalimab starting on Day15 (240 mg, q3w). Preoperative assessment will be performed two weeks (week 8) before surgery (week 10). In part 1 of the study, 6 patients will be enrolled to determine the safety and feasibility of the combination therapy. Subjects will be followed up for 90 days to observe perioperative adverse events. If the rate of delayed surgery (delay time >37 days) is >90% or the rate of grade 3/4 adverse effects is >70%, the study will be terminated. If not, 24 patients will be enrolled in part 2 of the study. This study is currently open and accruing patients.

REFERENCES

1. Cascone T, William WN Jr, Weissferdt A, et al. Neoadjuvant nivolumab or nivolumab plus ipilimumab in operable non-small cell lung cancer: the phase 2 randomized NEOSTAR trial. *Nat Med* 2021;**27**(3):504–514.
2. Provencio M, Nadal E, Insa A, et al. Neoadjuvant chemotherapy and nivolumab in resectable non-small-cell lung cancer (NADIM): an open-label, multicentre, single-arm, phase 2 trial. *Lancet Oncol* 2020 Nov;**21**(11):1413–1422.
3. Forde PM, Chaft JE, Smith KN, et al. Neoadjuvant PD-1 Blockade in Resectable Lung Cancer. *N Engl J Med* 2018 May 24;**378**(21):1976–1986.
4. Liu J, Blake SJ, Yong MC, et al. Improved efficacy of neoadjuvant compared to adjuvant immunotherapy to eradicate metastatic disease. *Cancer Discov* 2016;**6**:1382–99.
5. Pless M, Stupp R, Ris HB, et al. Induction chemoradiation in stage IIIA/N2 non-small-cell lung cancer: a phase 3 randomised trial. *Lancet* 2015 12;**386**(9998):1049–56.
6. Lemmon C, Videtic GM. M, Murthy SC, et al. A phase I safety and feasibility study of neoadjuvant chemoradiation plus pembrolizumab followed by

consolidation pembrolizumab in resectable stage IIIA non-small cell lung cancer. *J Clin Oncol* 2020; **38** (suppl; abstr 9009).

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.467>