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Neoadjuvant toripalimab plus chemotherapy with or without tifcemalimab (anti-BTLA antibody) in potentially resectable stage III non-small cell lung cancer (LungMate-014): A randomized, phase II trial

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Background

Perioperative toripalimab plus chemotherapy has improved outcomes in resectable stage III non-small cell lung cancer (NSCLC), and tifcemalimab combined with toripalimab has shown promising activity in advanced disease. Here, we first evaluated the addition of tifcemalimab to neoadjuvant toripalimab plus chemotherapy in patients with potentially resectable stage III NSCLC.

Methods

In this open-label, single-center, phase II trial, patients with potentially resectable disease were randomized 1:1 to receive toripalimab plus chemotherapy with tifcemalimab (TCT) or without tifcemalimab (TC) for 4 cycles. Surgical resectability was reassessed by multidisciplinary discussion. The primary endpoint was pathological complete response (pCR). Secondary endpoints included major pathological response (MPR), objective response rate (ORR), R0 resection, safety, event-free survival (EFS) and overall survival (OS).

Results

As of August 29, 2024, 118 patients were randomized in two arms. Patient characteristics were well balanced between the arms. pCR rates were 32.2% vs. 25.4% in the TCT and TC arms, respectively. Subgroup analyses showed higher pCR rates in patients with non-squamous histology (31.6% vs. 15.0%) and those with PD-L1 TPS <1% (35.7% vs. 25.9%). Surgery was performed in 67.8% and 59.3% of patients in the TCT and TC arms, with all achieving R0 resection. Grade ≥3 TRAEs occurred in 77.6% and 75.4% of patients, with no new safety signals. At a median follow-up of 26.6 months, 24-month EFS rates were 71.1% vs. 66.0%, and 24-month OS rates were 83.0% vs. 76.1% in the TCT and TC arms. Subgroup analyses suggested a trend toward improved survival in patients with non-squamous histology (24-month OS: 89.5% vs. 79.4%) and those with PD-L1 TPS <1% (24-month OS: 88.1% vs. 69.6%).

Conclusions

The addition of tifcemalimab to neoadjuvant toripalimab plus chemotherapy showed encouraging efficacy and manageable safety in potentially resectable stage III NSCLC. Notably, this strategy revealed enhanced benefit in patients with non-squamous histology and those with PD-L1 TPS <1%, supporting further evaluation in larger randomized trials.

Clinical trial identification

NCT05891080, first posted on June 6, 2023.

Legal entity responsible for the study

Shanghai Pulmonary Hospital.

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Disclosure

All authors have declared no conflicts of interest.

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