

A PHASE 2 STUDY OF TORIPALIMAB PLUS ANLOTINIB AS MAINTENANCE THERAPY IN EXTENSIVE-STAGE SMALL CELL LUNG CANCER

Dongqing Lv, Guixian Wu*. Taizhou Hospital of Zhejiang Province, Taizhou, China

Background Maintenance therapy is a promising therapeutic approach for extensive-stage small cell lung cancer (ES-SCLC), especially in light of IMpower 133.¹ The results of E3501, SALUTE and CALGB 30306 trials showed that in the first-line treatment of ES-SCLC, bevacizumab combined with chemotherapy improved only progression-free survival (PFS) but not overall survival (OS).^{2–4} Recent studies supported that combination of PD-1/PD-L1 immune checkpoint inhibitors (ICIs) and anti-angiogenic agents could be a promising therapeutic strategy for normalization of the immunosuppressive microenvironment and overcoming the low efficacy of ICIs.^{5–6} Toripalimab is a novel PD-1 inhibitor, combining with anlotinib as maintenance therapy for ES-SCLC may improve disease control.

Methods The eligible ES-SCLC patients with measurable target lesion (RECIST v1.1), ECOG performance status 0 or 1 and required to have complete response, partial response or stable disease per RECIST 1.1 following 4 to 6 cycles of platinum-based chemotherapy. 20 participants will be enrolled to receive maintenance therapy with toripalimab (240mg, IV, Q3W) and anlotinib (12mg, QD, Q3W) until disease progression, unacceptable toxicity or up to 2 years. Prophylactic cranial irradiation (PCI) was permitted at the investigator's discretion. The primary endpoints are the progression-free survival (PFS) and overall survival(OS). Secondary endpoints include safety, objective response rate (ORR), disease control rate (DCR) and time to response (TTR).

Results Between April, 2020, and June, 2021, 11 extensive-stage small cell lung cancer (ES-SCLC) patients (10 males, 1 females) were enrolled in the study: both of them completed four to six cycles chemotherapy, 11 (100%) achieved a best response of disease control (partial response or stable disease). The median age was 66 (range, 53–78) years. As of June 30, 2021 (data cutoff date), the median follow-up was 4.6 months. The median PFS had not been reached (range, 1.4+ to 14.5+ month). One (1/11) patients had disease progression after 7 months of maintenance treatment. All patients were still alive, and the median OS had not been reached. 90.9% (10/11) patients were still receiving treatment. The most common adverse events (AEs) were grade 1–2 rash (17.2%), decreased appetite (13.8%), leucopenia (6.9%), and Myalgia (6.9%). Two patients had herpes zoster, treatment with ICIs may result in varicella-zoster reactivation. Four patients had Grade 3 AEs (1 pneumonitis 2 hypothyroidism; 1 rash, and 1 myalgia). No grade 4/5 AEs occurred.

Conclusions In this phase 2 study, patients with ES-SCLC who continued toripalimab with anlotinib as maintenance therapy after induction therapy with etoposide-platinum chemotherapy showed promising anti-tumor activity and tolerable toxicities.

Trial Registration Clinical trial information: NCT04363255.

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Ethics Approval Ethics approval was granted by Committee of Enze Hospital of Taizhou Enze Medical (Center NO. K20200402)

Consent Informed written consent for publication was obtained from the patient prior to collecting information. The patient gave written consent for personal or clinical details along with any identifying images to be published in this study.

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