Non-small-cell lung

Sugemalimab versus placebo after concurrent or sequential chemoradiotherapy in patients with locally advanced, unresectable, stage III non-small-cell lung cancer in China (GEMSTONE-301): interim results of a randomised, double-blind, multicentre, phase III trial

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BACKGROUND

A substantial proportion of patients with unresectable stage III non-small-cell lung cancer (NSCLC) cannot either tolerate or access concurrent chemoradiotherapy, so sequential chemoradiotherapy is commonly used. We assessed the efficacy and safety of sugemalimab, an anti-PD-L1 antibody, in patients with stage III NSCLC whose disease had not progressed after concurrent or sequential chemoradiotherapy.

METHODS

GEMSTONE-301 is a randomised, double-blind, placebo-controlled, phase III trial in patients with locally advanced, unresectable, stage III NSCLC, done at 50 hospitals or academic research centres in China. Eligible patients were aged 18 years or older with an Eastern Cooperative Oncology Group (ECOG) performance status of 0.0 or 1.0 who had not progressed after concurrent or sequential chemoradiotherapy. We randomly assigned patients (2:1, using an interactive voice-web response system) to receive sugemalimab 1200 mg or matching placebo, intravenously every three weeks for up to 24 months. Stratification factors were ECOG performance status, previous chemoradiotherapy, and total radiotherapy dose. The investigators, trial coordination staff, patients, and study sponsor were masked to treatment allocation. The primary endpoint was progression-free survival as assessed by blinded independent central review (BICR) in the intention-to-treat population. Safety was assessed in all participants who received at least one dose of assigned study treatment. The study has completed enrolment and the results of a preplanned analysis of the primary endpoint are reported here. The trial is registered with ClinicalTrials.gov, NCT03728556.

FINDINGS

Between 30 Aug 2018 and 30 Dec 2020, we screened 564 patients of whom 381 were eligible. Study treatment was received by all patients randomly assigned to sugemalimab (n=255) and to placebo (n=126). At data cutoff (8 March 2021), median follow-up was 14·3 months (IQR 6·4-19·4) for patients in the sugemalimab group and 13·7 months (7·1-18·4) for patients in the placebo group. Progression-free survival assessed by BICR was significantly longer with sugemalimab than with placebo (median 9·0 months [95% CI 8·1-14·1] vs 5·8 months [95% CI 4·2-6·6]; stratified hazard ratio 0·64 [95% CI 0·48-0·85], p=0·0026). Grade 3.0 or 4.0 treatment-related adverse events occurred in 22 (9%) of 255 patients in the sugemalimab group versus seven (6%) of 126 patients in the placebo group, the most common being pneumonitis or immune-mediated pneumonitis (seven [3.0%] of 255 patients in the sugemalimab group vs one [<1.0%] of 126 in the placebo group). Treatment-related serious adverse events occurred in 38 (15%) patients in the sugemalimab group and 12 (10%) in the placebo group. Treatment-related deaths were reported in four (2.0%) of

255 patients (pneumonia in two patients, pneumonia with immune-mediated pneumonitis in one patient, and acute hepatic failure in one patient) in the sugemalimab group and none in the placebo group.

INTERPRETATION

Sugemalimab after definitive concurrent or sequential chemoradiotherapy could be an effective consolidation therapy for patients with stage III NSCLC whose disease has not progressed after sequential or concurrent chemoradiotherapy. Longer follow-up is needed to confirm this conclusion.