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Chemo-immunotherapy followed by durvalumab and ceralasertib in treatment naïve patients with extensive-stage small cell lung cancer

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Background

Extensive stage small cell lung cancer (ES-SCLC) is initially responsive to therapy; however, most patients relapse with a median overall survival (OS) of 13 months. Maintaining the response achieved during the first-line of therapy may improve outcomes. Ceralasertib, an ataxia-telangiectasia and Rad3-related (ATR) inhibitor, can target SCLC dependency on the DNA damage response and remodel the tumor microenvironment to drive durability of response.

Methods

A multicenter single arm phase II study was conducted to evaluate the efficacy of adding ceralasertib to maintenance durvalumab (CD) after induction with platinum-etoposide and durvalumab (PED) in patients with treatment naïve ES-SCLC. Patients were enrolled prior to initiating PED. The primary endpoint was progression-free survival (PFS). All outcomes were assessed from the time of enrollment. Patients without progression after four cycles of PED, initiated ceralasertib at 240 mg twice daily on days 1-7 with durvalumab on day 8 in a 28-day cycle, until progression.

Results

Thirty patients were enrolled between Aug 2021 and Feb 2024 with a median follow-up of 13.5 months. The median age was 65 years. The majority were female (56.7%), White (82.1%), and ECOG PS of 1(73.3%). Twenty-five patients (83.3%) received ≥ 1 cycle of CD. The confirmed overall response rate was 73.3% (n=22) with two complete responses. The median duration of response was 6.6 months (95% CI 3.9, 17.1). The best overall response for two patients (6.7%) was progression. The median PFS was 6.1 months (95% CI 4.8, 9.5). Median overall survival (OS) had not been reached, but 12- and 24-month OS rates were 68% (95% CI 48, 82) and 59% (95% CI 37, 75), respectively. Grade 3-4 treatment emergent adverse events occurring in ≥ 10% of patients included neutropenia (26.7%), fatigue (20%), anemia (16.7%), infection (13.4%), and dyspnea (10%). Fourteen patients (46.7%) developed serious adverse events, of which seven (50%) were treatment related.

Conclusions

The combination of chemo-immunotherapy followed by ceralasertib and durvalumab has shown promising efficacy with higher rates of 12- and 24-month survival over that expected for durvalumab maintenance alone, and did not show any new safety signal.

Clinical trial identification

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Legal entity responsible for the study

Big Ten Cancer Research Consortium, United States of America.

Funding

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Disclosure

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