First-line pembrolizumab or placebo combined with etoposide and platinum for ES-SCLC

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Long-term follow up of patients with extensive stage small cell lung cancer who were given pembrolizumab and etoposide/platinum (EP) versus placebo + etoposide/platinum as first-line therapy support the continued exploration of pembrolizumab-based combinations for patients with small cell lung cancer.

In the phase 3 KEYNOTE-604 study of pembrolizumab and etoposide/platinum (EP) versus placebo and etoposide/platinum as first-line therapy for ES-SCLC (NCT03066778), progression-free survival was significantly improved with pembrolizumab + EP versus placebo + EP (HR, 0.75 [95% CI, 0.61-0.91]; P=0.0023) and although the hazard ratio for overall survival favored pembrolizumab + EP, the significance threshold was not met (HR, 0.80 [95% CI, 0.64-0.98]; P=0.0164).

To build on this earlier study, Dr. Charles Rudin from Memorial Sloan Kettering Cancer Center in New York City presented updated results with a median of 3.5 years of follow-up and outcomes in patients who completed the maximum of 35 cycles of pembrolizumab on study.

In KEYNOTE-604, eligible patients with previously untreated ES-SCLC were randomized 1:1 to pembrolizumab 200 mg or placebo for up to 35 cycles plus four cycles of standard-dose EP. Dual primary endpoints were overall survival and progression-free survival (RECISTv1.1, blinded central review) in the intent-to-treat (ITT) population.

Of the 453 randomized patients in the ITT population (pembrolizumab + EP, n=228; placebo + EP, n=225), median (range) time from randomization to data cutoff (September 21, 2021) was 43.3 (37.8-52.3) months. 54.8% of patients in the pembrolizumab + EP group and 66.2% in the placebo + EP group received subsequent therapy (11.2% vs 22.1% received subsequent immune checkpoint inhibitor). Efficacy outcomes, including overall survival and progression-free survival, were improved with pembrolizumab + EP. 3-year overall survival was 15.5% among patients treated with pembrolizumab + EP vs. 5.9% in those treated with placebo + EP. Grade 3-5 adverse events occurred in 78.9% of patients in the pembrolizumab + EP group and 77.1% of patients in the placebo + EP group. Eighteen patients completed 35 cycles of pembrolizumab (median [range] time from randomization to database cutoff, 42.5 [38.2-49.5] months); of these patients, 14 were alive as of the last assessment before data cutoff. ORR among these patients was 100% (95% CI, 81.5%-100%; 2 CR, 16 PR), and median (range) DOR was not reached (14.1 to 46.8+ months). From the time of completing 35 cycles (~2 years), median OS was not reached (95% CI, 16.6 months to not reached). Two-year OS rate (95% CI) from the time of completing 35 cycles of pembrolizumab was 72.2% (39.5%-89.2%).

"Pembrolizumab and EP continued to show clinically meaningful improvement in survival and manageable safety versus placebo + EP in patients with previously untreated ES-SCLC; 3-year overall survival rate was over two and a half times higher among patients who received pembrolizumab and EP," Dr. Rudin reported. "Patients who completed 35 cycles of pembrolizumab had durable responses. Data support the continued exploration of pembrolizumab-based combinations for patients with small cell lung cancer."

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