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Adding ipilimumab to pembrolizumab does not improve efficacy in patients with NSCLC

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Adding ipilimumab to pembrolizumab does not improve efficacy and is associated with greater toxicity than pembrolizumab alone as first-line therapy for metastatic non-small cell lung cancer (NSCLC) for patients with a PD-L1 tumor proportion score of greater than or equal to 50% and no targetable EGFR or ALK aberrations, according to research presented today at the International Association for the Study of Lung Cancer's World Conference on Lung Cancer.

The research was presented by Dr. Michael Boyer, clinical professor of medicine at the Chris O'Brien Lifehouse and the Central Clinical School of the University of Sydney, Sydney, Australia.

Previously, the KEYNOTE-024 study showed that pembrolizumab monotherapy significantly improved survival versus platinum-doublet chemotherapy for patients with metastatic NSCLC, a PD-L1 TPS greater than or equal to 50%, and no targetable EGFR or ALK aberrations.

Boyer and his research group, which consisted of centers in Europe, Asia, and North America, conducted the randomized, double-blind, phase III KEYNOTE-598 study (NCT03302234) to determine whether adding ipilimumab to pembrolizumab improved efficacy over pembrolizumab alone in this population.

The trial enrolled 568 participants—284 received a combination of pembrolizumab and ipilimumab and 284 were randomly assigned to

receive pembrolizumab and placebo.

Patients were randomly assigned 1:1 to ipilimumab at 1 mg/kg every six weeks or to saline placebo for up to 18 cycles. Patients in both arms received 200 mg of pembrolizumab every three weeks for up to 35 cycles. Random assignment was stratified by European Cooperative Oncology Group score of (0 vs 1), region (East Asia vs not East Asia), and histology (squamous vs nonsquamous). Treatment differences in the primary endpoints of overall survival and progress-free survival were assessed by the stratified log-rank test in the intent-to-treat population.

The protocol-specified first interim analysis (IA1) was planned to occur when approximately 255 deaths occurred and approximately 12 months had passed since the last participant was randomly assigned. Nonbinding futility criteria at IA1 were differences in the restricted mean survival time between ipilimumab/pembrolizumab and placebo/pembrolizumab of less than or equal to 0.2 at the maximum observation time and less than or equal to 0.1 at 24 months of follow-up.

With 272 deaths, median overall survival was 21.4 months for patients who received ipilimumab/pembrolizumab compared to 21.9 months for placebo/pembrolizumab (HR, 1.08 ;95% CI: 0.85-1.37; p = 0.74). Restricted mean survival time differences were -0.56 at the maximum observation time and -0.52 at 24 months, which met the futility criteria, according to Dr. Boyer.

With 372 events, median progression-free survival was 8.2 months for the ipilimumab/pembrolizumab group compared with 8.4 months for placebo/pembrolizumab (HR, 1.06; 95% CI: 0.86-1.30; p = 0.72). The objective response rate was 45.4% in both arms; median duration of response was 16.1 months for the ipilimumab/pembrolizumab group vs 17.3 months for placebo/pembrolizumab. Treatment-related adverse events occurred in 76.2% of patients in the ipilimumab/pembrolizumab

group versus 68.3% for the placebo group.

Dr. Boyer reported that based on the observed efficacy and safety, the external data monitoring committee recommended that the study be stopped due to futility and that participants discontinue both ipilimumab and placebo.

"As a consequence of the results of this study, monotherapy with pembrolizumab remains a standard of care for this population of patients. Despite the benefits of this type of treatment, almost 50% of these patients die of their disease within two years, so future research will focus on other ways to improve outcomes," he reported.

Provided by International Association for the Study of Lung Cancer

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