Association between KRAS/STK11/KEAP1 mutations and outcomes in POSEIDON

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Patients with metastatic non-small cell lung cancer who received a combined therapy of tremelimumab, durvalumab and chemotherapy experienced longer overall survival compared with those who received chemotherapy alone, regardless of STK11, KEAP1 or KRAS mutational status, according to research from the POSEIDON trial presented at the IASLC World Conference on Lung Cancer 2022 in Vienna.

In previously reported results of the phase 3 POSEIDON trial, patients with EGFR/ALK wild-type metastatic NSCLC who were given first-line tremelimumab, durvalumab and chemotherapy demonstrated statistically significant improvements in both progression-free survival and overall survival versus chemotherapy alone.

CTLA-4 inhibition supports T-cell expansion; PD-L1 inhibition overcomes T-cell suppression at the tumor; and chemotherapy causes tumor cell death and antigen release, potentially priming the immune response. Mutations in STK11 and KEAP1 correlate with poor prognosis and are associated with chemorefractory and immunologically "cold" tumors that are less responsive to therapy. KRAS mutant NSCLC is heterogenous and frequently co-mutated with STK11 and/or KEAP1. Based on these findings, researchers theorized that the triplet regimen tremelimumab, durvalumab and chemotherapy may improve clinical outcomes for hard-to-treat subgroups of patients with metastatic NSCLC.

Dr. Solange Peters, Centre Hospitalier Universitaire Vaudois, Lausanne

University, Switzerland and colleagues conducted an exploratory analyses of survival outcomes in POSEIDON according to KRAS, STK11 and KEAP1 mutational status.

Dr. Peters and researchers at study locations randomized 1013 patients (1:1:1) to first-line tremelimumab, durvalumab and chemotherapy; durvalumab and chemotherapy; or just chemotherapy, with stratification by tumor cell PD-L1 expression (≥50% vs