Mutations associated with sensitivity or resistance to immunotherapy in mNSCLC

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The relationship between gene alterations and response to anti-PD-L1 with and without anti-CTLA-4 are not well characterized. Dr. N. Rizvi from Columbia University Medical Center in New York today presented an update from the Phase III MYSTIC study that showed poorer outcomes across treatment arms in patients with metastatic non-small cell lung cancer and mutations in STK11 or KEAP1 genes compared with those without the corresponding mutations. In patients receiving durvalumab with tremelimumab, ARID1Am was associated with survival benefits compared with ARID1Awt.

Rizvi presented his data today at the IASLC 2019 Word Conference on Lung Cancer hosted by the International Association for the Study of Lung Cancer.

The MYSTIC trial is a randomized, open-label, multi-center, global Phase III trial of durvalumab monotherapy or durvalumab in combination with tremelimumab versus chemotherapy in the 1st-line treatment of patients with epidermal growth factor receptor and anaplastic lymphoma kinase wild-type, locally-advanced or metastatic non-small cell lung cancer. The trial was conducted at 203 sites in 17 countries. Previously, according to research published in the American Association of Cancer Research, blood tumor mutational burden, at various thresholds from greater to or equal to 12 mut/Mb to >20 mut/Mb, has been associated with improved overall survival with first-line durvalumab with or without tremelimumab versus chemotherapy.

In the current exploratory analysis, researchers obtained circulating tumor DNA from baseline plasma specimens from 1003 patients which was then profiled using the GuardantOMNI platform. Survival outcomes were analyzed in those with (designation with m) and without (wt) non-synonymous somatic mutations.

In the mutation-evaluable population (n=943), STK11 mutation, KEAP1 mutation, and ARID1A mutation frequencies were 16 percent, 18 percent and 12 percent, respectively (19 percent, 20 percent, and 11 percent [nonsquamous]; 7 percent, 13 percent, and 15 percent [squamous]).

Across treatment arms, patients with STK11m or KEAP1m had a shorter median overall survival than patients with STK11wt or KEAP1wt metastatic NSCLC. In the durvalumab + tremelimumab arm, patients with ARID1A mutations had a longer median overall survival rate than patients with ARID1A without mNSCLC.

Provided by International Association for the Study of Lung Cancer