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Mutations Associated with Sensitivity or Resistance to Immunotherapy in mNSCLC: Analysis from the MYSTIC Trial

Barcelona—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, *ARID1A*m was associated with survival benefits compared with *ARID1A*wt.

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 *STK11*m or *KEAP1*m had a shorter median overall survival than patients with *STK11*wt or *KEAP1*wt metastatic NSCLC. In the durvalumab + tremelimumab arm, patients with *ARID1A* mutations had a longer median overall survival rate than patients with *ARID1A* without mNSCLC.

About the WCLC:

The WCLC is the world's largest meeting dedicated to lung cancer and other thoracic malignancies, attracting more than 7,000 researchers, physicians and specialists from more than 100 countries. The goal is to increase awareness, collaboration and understanding of lung cancer, and to help participants implement the latest developments across the globe. The conference will cover a wide range of disciplines and unveil several research studies and clinical trial results. For more information, visit wclc2019.iaslc.org.

About the IASLC:

The International Association for the Study of Lung Cancer (IASLC) is the only global organization dedicated solely to the study of lung cancer and other thoracic malignancies. Founded in 1974, the association's membership includes more than 7,500 lung cancer specialists across all disciplines in over 100 countries, forming a global network working together to conquer lung and thoracic cancers worldwide. The association also publishes the *Journal of Thoracic Oncology*, the primary educational and informational publication for topics relevant to the prevention, detection, diagnosis and treatment of all thoracic malignancies. Visit www.iaslc.org for more information.

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