Clinical trial shows durvalumab plus ceralasertib boosted immune response in lung cancer patients

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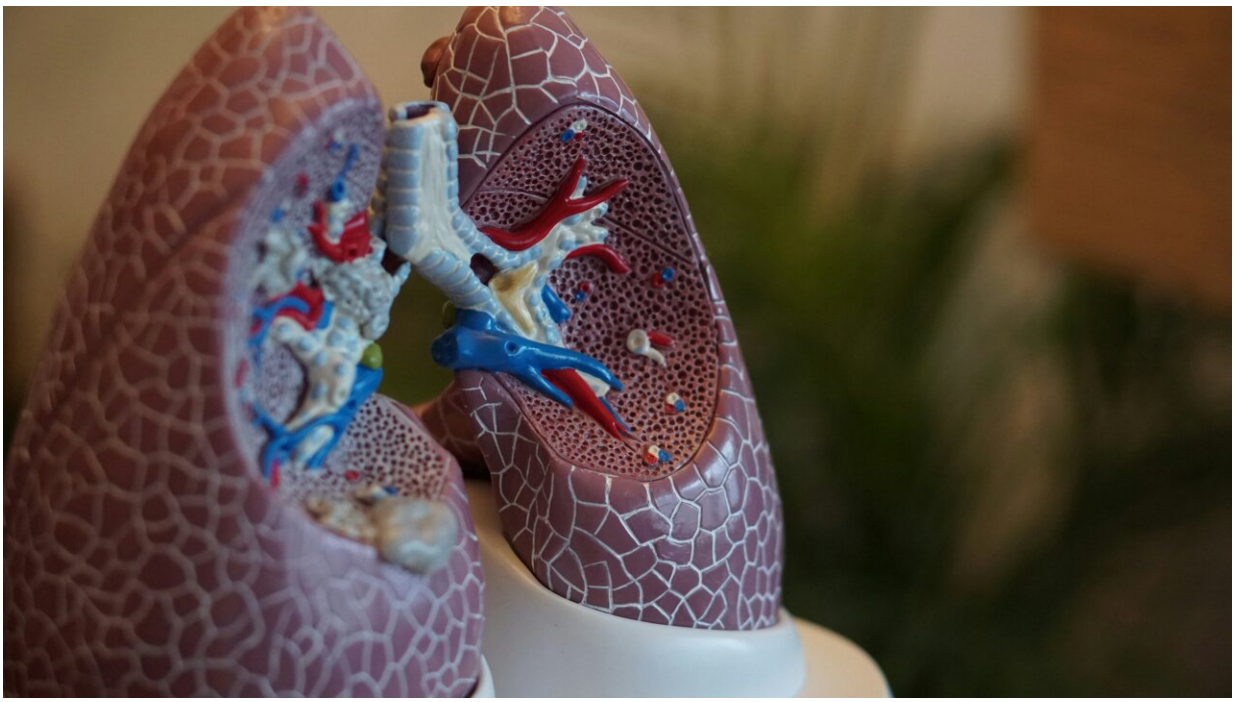

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A specific combination of targeted therapy and immunotherapy may better help patients with non-small cell lung cancer (NSCLC) overcome inherent immune resistance and reinvigorate anti-tumor activity, according to a new study led by a researcher from The University of

Texas MD Anderson Cancer Center.

Results from the Phase II umbrella HUDSON study, published in Nature Medicine, demonstrate that the anti PD-L1 antibody, durvalumab, coupled with the ATR inhibitor, ceralasertib, provides the greatest clinical benefit of four combinations evaluated.

This pair had an objective response rate (ORR) of 13.9% compared to just 2.6% with the other tested combinations. Median progression-free survival (PFS) was 5.8 months versus 2.7 months for other combinations, while median overall survival (OS) was 17.4 months versus 9.4 months. In patients with ATM alterations, which should sensitize tumors to ATR inhibitors, the ORR increased to 26.1%. Durvalumab-ceralasertib had a manageable safety profile.

"Patients with advanced non-small cell lung cancer face significant challenges when standard-of-care treatments fail," said corresponding author John Heymach, M.D., Ph.D., chair of Thoracic/Head & Neck Medical Oncology.

"For these individuals, options become limited, emphasizing the urgent need for innovative approaches. Our study represents a promising advancement in addressing this unmet need and holds the potential to offer more effective therapeutic strategies to improve outcomes for this population."

This study enrolled 268 patients with advanced NSCLC who progressed following standard-of-care therapy. The median age of participants was 63–64 years; 58% were male.

Patients on the trial received one of four targeted therapies in combination with durvalumab: ceralasertib (ATR kinase inhibitor), olaparib (PARP inhibitor), danvatirsen (STAT3 antisense

oligonucleotide) or oleclumab (anti-CD73 monoclonal antibody).

Tumor molecular characteristics were analyzed before treatment, and patients were categorized into biomarker-matched or -unmatched treatment cohorts based on ATM alterations, homologous recombination repair defects, STK11/LKB1 alterations, or high CD73 expression.

Based on the results, durvalumab plus ceralasertib is now being tested in a randomized Phase III trial for patients with immunotherapy-refractory NSCLC.

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