Clinical trial: Combining durvalumab with novel agents increases pathological responses in resectable NSCLC

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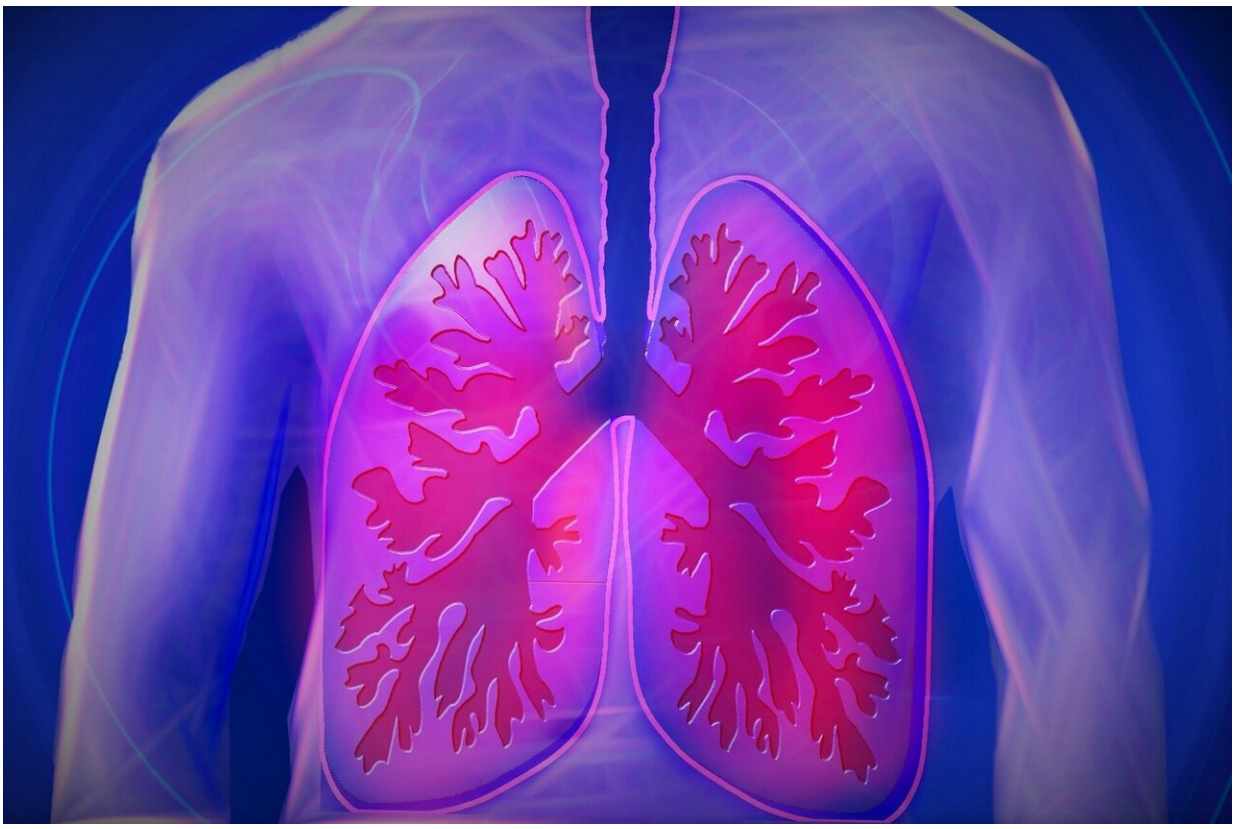

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Phase 2 results from the NeoCOAST-2 study have demonstrated that the combination of durvalumab with Dato-DXd yielded the highest

pathological complete response rates among the tested regimens.

The data was presented at the International Association for the Study of Lung Cancer (IASLC) 2024 World Conference on Lung Cancer by Dr. Tina Cascone, from The University of Texas MD Anderson Cancer Center in Houston.

"The findings highlight the potential of combining durvalumab with novel anticancer agents to build on what we have learned in the perioperative immunotherapy arena for patients with early-stage, resectable NSCLC to enhance treatment outcomes and safety profiles," Dr. Cascone reported.

The NeoCOAST-2 study is an open-label, multicenter Phase 2 trial that builds on the results of the NeoCOAST and AEGEAN studies as foundation for evaluating the efficacy of durvalumab combined with chemotherapy and novel agents as neoadjuvant therapy, followed by adjuvant therapy with durvalumab alone or with additional agents. The study aimed to improve pathological complete response (pCR) rates in patients with resectable NSCLC.

The study enrolled patients with untreated, histologically confirmed Stage IIA-IIIB NSCLC, stratified by PD-L1 expression, and randomized them into several arms, including the three reported arms:

- Arm 1: Neoadjuvant durvalumab and platinum-doublet CT with oleclumab
- Arm 2: Neoadjuvant durvalumab and platinum-doublet CT with monalizumab
- Arm 4: Neoadjuvant durvalumab and single-agent platinum CT with Dato-DXd (TROP2-directed antibody-drug conjugate).

Patients received neoadjuvant therapy every three weeks for four cycles

prior to surgery, followed by adjuvant treatment with the respective regimens until disease progression or up to one year. Primary endpoints included pCR rate, safety, and tolerability, while secondary endpoints covered event-free survival, feasibility of surgery, major pathological response (mPR) rate, and objective response rate.

Dr. Cascone and her colleagues randomized 202 patients (Arm 1: n=76; Arm 2: n=72; Arm 4: n=54). Of those, 92.2%, 92.1%, and 95.8% of patients in Arms 1, 2, and 4, respectively, underwent surgery. The pCR rates were 20%, 26.7%, and 34.1% for Arms 1, 2, and 4, respectively, with corresponding mPR rates of 45%, 53.3%, and 65.9%. Arm 4 showed the highest pCR rate and a generally favorable safety profile. Treatment-related adverse events (TRAEs) occurred in 94.6% of patients in Arm 1, 90.1% in Arm 2, and 96.3% in Arm 4, with grade ≥3 TRAEs reported at 31.1%, 29.6%, and 18.5%, respectively.

"The NeoCOAST-2 study is the first global Phase 2 platform trial to provide evidence that the combination of durvalumab with novel agents, particularly Dato-DXd, yields the highest rates of pathological complete response among the tested regimens," said Dr. Cascone.

"This promising efficacy, coupled with a manageable safety profile, underscores the potential of these novel treatment combinations in improving outcomes for patients with resectable NSCLC, and the results affirm the viability of integrating novel anticancer agents into neoadjuvant and perioperative therapy for enhanced clinical benefit."

Provided by International Association for the Study of Lung Cancer