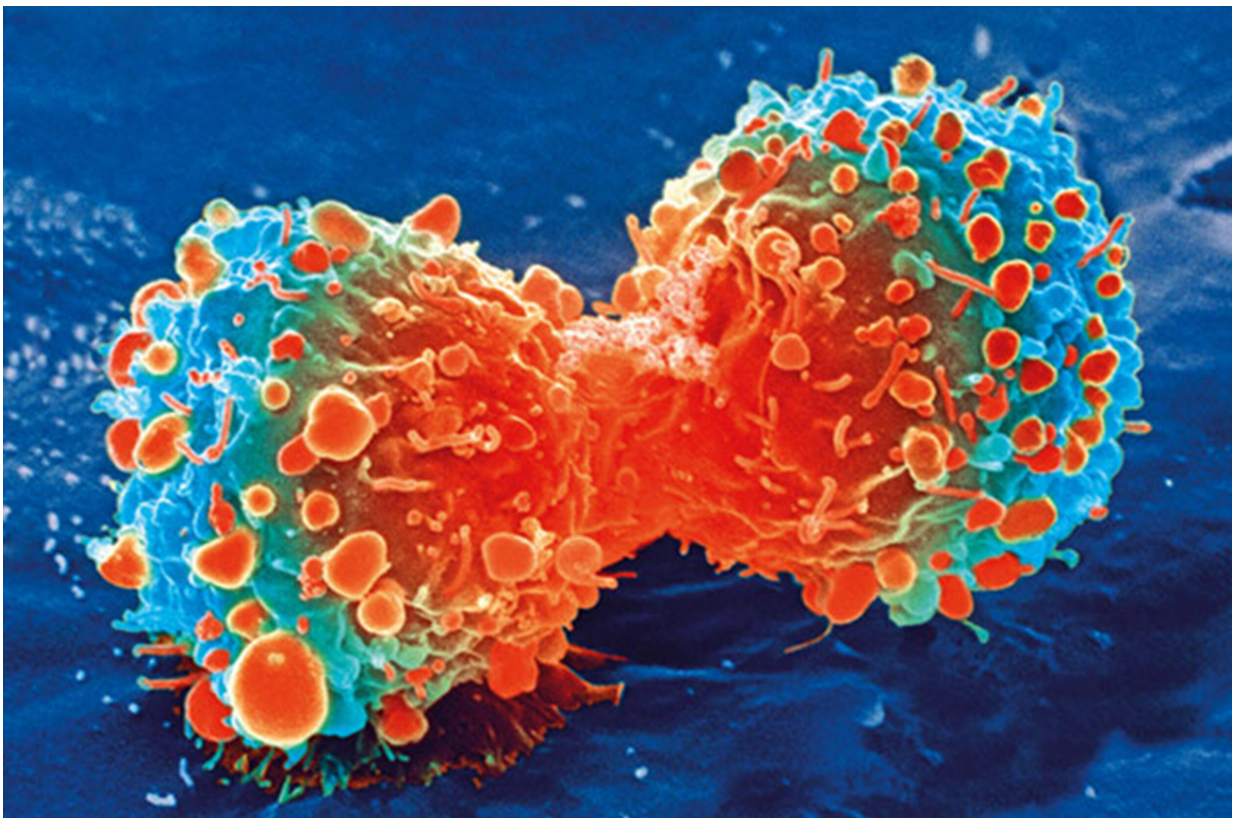


Neoadjuvant combination immunotherapy improves outcomes for early stage non-small cell lung cancer

February 18 2021



Cancer cell during cell division. Credit: National Institutes of Health

The first randomized Phase II clinical trial to report on single and combined neoadjuvant immune checkpoint inhibitor therapy in stage I-

III non-small cell lung cancer (NSCLC) found combination therapy produced a significant clinical benefit, as assessed by major pathologic response (MPR) rate, as well as enhanced tumor immune cell infiltration and immunological memory. Researchers from The University of Texas MD Anderson Cancer Center published the study results today in *Nature Medicine*.

The NEOSTAR trial tested combined neoadjuvant therapy of nivolumab plus ipilimumab, as well as neoadjuvant nivolumab monotherapy in [patients](#) with operable NSCLC. The trial met its prespecified primary endpoint efficacy threshold in the combination arm, with eight of 21 treated patients (38%) achieving major pathological response, defined as $\geq 10\%$ viable tumor at surgery. MPR has been shown to correlate with improved survival outcomes after neoadjuvant chemotherapy in NSCLC. The prespecified efficacy boundary for each treatment to be considered promising for further testing was six or more MPRs in 21 evaluable patients. With MPR in five of 23 treated patients (22%), monotherapy did not meet the efficacy boundary.

While combination immunotherapy has been approved for a subset of patients with metastatic NSCLC, this is the first randomized study to report on the role of combination checkpoint inhibitors for operable, early stage disease.

"More than 50% of patients with localized non-[small cell lung cancer](#) will relapse if treated with surgery alone. Adding chemotherapy produces only a modest improvement in overall survival, and it comes with toxicity," said Tina Cascone, MD., Ph.D., assistant professor of Thoracic/Head & Neck Medical Oncology and lead author of the study. "The results from our study with neoadjuvant combination immunotherapy are particularly encouraging in that we found that this dual treatment can induce higher pathologic responses and trigger immunological memory. This may translate into a reduced risk for tumor

relapse in more patients with early stage non-small cell lung cancer."

Study design and secondary endpoints

The Phase II single-institution study enrolled 44 patients with surgically resectable stage IA to IIIA NSCLC between June 2017 and November 2018. The median age of trial participants was 66 years old, and 64% were male. Participants were 84% white, 9% Black and 5% Asian. Most participants had a history of smoking: 23% identified as current smokers and 59% as former smokers.

Patients were randomized to one of two treatment arms with immune checkpoint inhibitors prior to surgery: 23 received three doses of nivolumab alone and 21 received three doses of nivolumab plus one dose of ipilimumab. Each arm was compared against historical controls of neoadjuvant chemotherapy. Overall, 41 patients completed the planned three doses of therapies, 37 patients had surgery on trial and two patients underwent surgery off trial after additional therapies.

Among the 37 patients who had surgical resection on the study, the combination arm showed higher MPR rates (50% versus 24%) and fewer viable tumor cells at resection than monotherapy (a median of 9% versus 50%). Combination therapy also showed better pathological complete response rates than monotherapy (38% versus 10%). After a median follow-up of 22 months, median overall survival and lung cancer-related recurrence-free survival were not reached.

Toxicities were manageable overall, with no new safety concerns compared to known adverse event profiles of either drug. The median time to surgery was 31 days after the last dose of nivolumab. Some patients experienced nodal immune flare (NIF), or the appearance of nodal disease progression on radiographic imaging, which invasive node biopsy revealed to be immune cell infiltration rather than malignant

disease.

Exploratory analyses reveal immune impact, potential biomarkers

In an exploratory analysis of resected tissues, investigators found—and reported for the first time—higher levels of immune cell infiltration in tumors treated with combination therapy, including an abundance of CD3+ and CD3+CD8+ T lymphocytes, tissue-resident memory and effector memory T cells. Tumors that responded better to treatment had higher PD-L1 expression at baseline, but responses were also observed in those without PD-L1 expression in tumor cells.

The researchers analyzed the gut microbiome, as well, and found that pathologic response to [combination therapy](#) was associated with the presence of certain fecal microbes that also have been correlated with immunotherapy response in melanoma and other cancers. Immune checkpoint inhibitor therapy did not significantly affect the diversity or composition of the microbiome in this study.

"Our exploratory results suggest the gut microbiome may play a role in responses to neoadjuvant immune checkpoint inhibitors in lung cancer," Cascone said. "The immune microenvironment findings also give us an opportunity to look at immune cell populations and potential biomarkers that can be evaluated in the future to identify those patients who are most likely to benefit from these agents in new prospective trials."

The NEOSTAR trial has been amended to a modular platform design, which provides the opportunity to add treatment arms to rapidly test and advance promising new neoadjuvant therapeutic combinations. Results from a third arm testing neoadjuvant nivolumab plus chemotherapy are expected later this year. A fourth arm testing the combination of dual

immunotherapy plus chemotherapy is ongoing.

"The NEOSTAR trial results set the stage for evaluating the role of dual immunotherapy added to neoadjuvant chemotherapy, which we are currently exploring, and expediting the investigation of novel agents in the perioperative setting," Cascone said. "This is a population with potentially curable disease. We should do whatever it takes to minimize the risk of relapse and increase the cure rates for these patients."

More information: Weissferdt, A. et al. Neoadjuvant nivolumab or nivolumab plus ipilimumab in operable non-small cell lung cancer: the phase 2 randomized NEOSTAR trial. Nat Med (2021).

doi.org/10.1038/s41591-020-01224-2

Provided by University of Texas M. D. Anderson Cancer Center

Citation: Neoadjuvant combination immunotherapy improves outcomes for early stage non-small cell lung cancer (2021, February 18) retrieved 23 April 2024 from <https://medicalxpress.com/news/2021-02-neoadjuvant-combination-immunotherapy-outcomes-early.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.