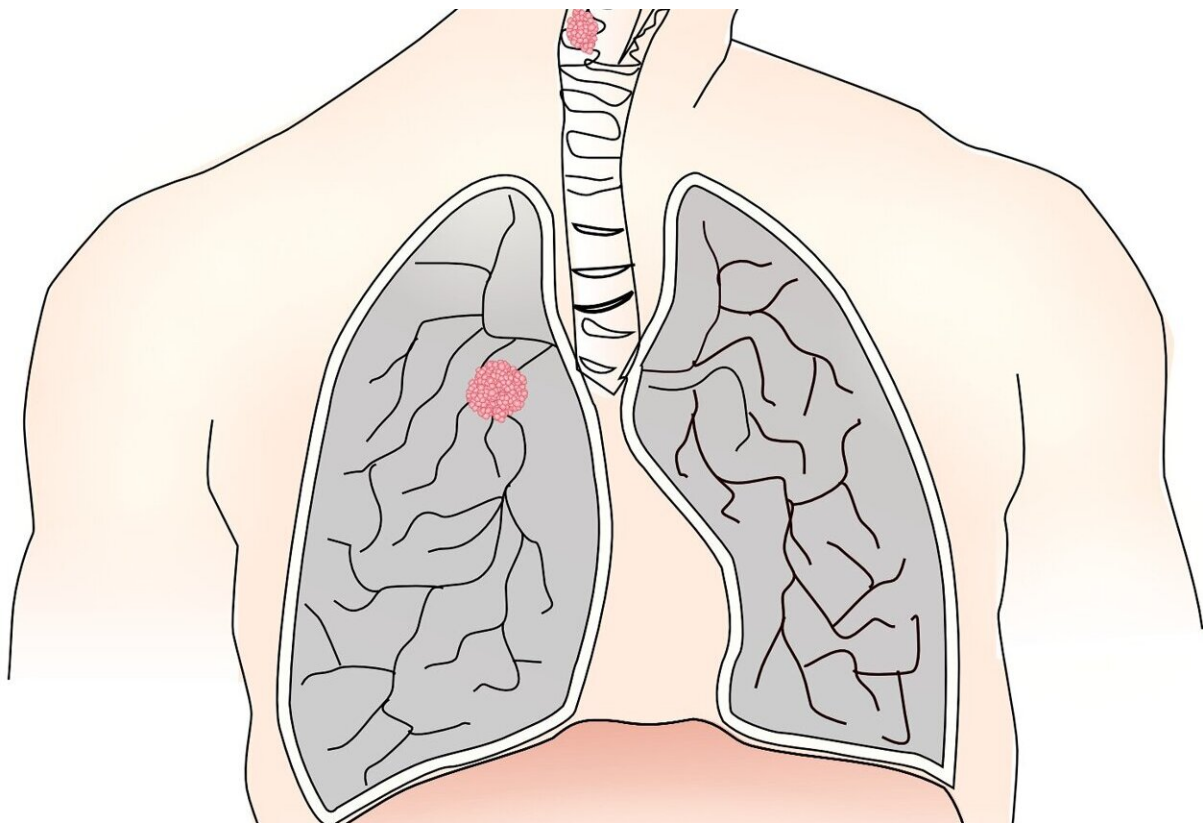


Combination cancer therapies can shrink tumors and improve outcome in advanced non-small lung cancer: Clinical trial

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While pembrolizumab is an approved treatment for patients with stage III non-small cell lung cancer (NSCLC), only some patients respond to

this therapy. Treatment failure, researchers say, is often caused by differences in the tumor microenvironment.

An ongoing phase II study (KEYNOTE-495/KeyImPaCT) led by a researcher at Yale Cancer Center reveals that combining pembrolizumab with other treatments reduced the size of target tumors, resulting in a higher response rate for patients with advanced NSCLC. The new research was published July 10 in *Nature Medicine*.

In this study, patients were categorized into four biomarker-defined groups based on their [gene expression](#) and amount of gene mutation in the [cancer cells](#). Essentially, patients were grouped by similar [tumor microenvironment](#). Patients in each of the four groups were then randomly assigned to receive pembrolizumab (also marketed under the name Keytruda) in combination with one of three other cancer treatments: lenvatinib (also known as Lenvima), quavonlimab, or favezelimab.

"The study's approach of categorizing patients into biomarker-defined subgroups allows us to identify potential unique resistance mechanisms and tailor treatment strategies accordingly," said Herbst.

The study assessed the objective response rate (ORR), or the percentage of patients who had a partial or complete response to the treatment, as well as [progression-free survival](#) (PFS), and safety.

The study reported ORR ranges of 0% to 12% in group I, 27.3% to 33.3% in group II, 13.6% to 40.9% in group III, and 50% to 60% in group IV, with ranges encompassing the results of the different treatment combinations. There was at least a 30% reduction in the target tumor size in more than 58% of patients in group IV. PFS was also highest for group IV, ranging from 6.3 months to 17.8 months. The most common treatment-related adverse events included hypertension, itchy

skin, and fatigue.

The interim results from the study showed that each of the treatment combinations provided anti-tumor activity, particularly in group IV. Additional research from the trial will provide further insight on optimal combinations targeting specific molecular subtypes in NSCLC and other tumor types.

"These findings reinforce the importance of personalized medicine in improving outcomes for [patients](#) with NSCLC and pave the way for further advancements in pembrolizumab combination therapies," said Herbst.

The first author was Dr. Martin Gutierrez at Hackensack University Medical Center.

More information: Martin Gutierrez et al, Biomarker-directed, pembrolizumab-based combination therapy in non-small cell lung cancer: phase 2 KEYNOTE-495/KeyImPaCT trial interim results, *Nature Medicine* (2023). [DOI: 10.1038/s41591-023-02385-6](https://doi.org/10.1038/s41591-023-02385-6)

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