Up-front Chemotherapy Boost Could Benefit Patients with Non-Small-Cell Lung Cancer

Adding chemotherapy to Tagrisso was associated with a nearly nine-month delay in disease progression—and more side effects.

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In a Phase 3 global clinical trial called FLAURA2 led by researchers from Dana-Farber Cancer Institute and Institut Gustav Roussy in France, patients with non-small-cell lung cancer (NSCLC) with an epidermal growth factor receptor (EGFR) mutation taking standard therapy plus chemotherapy had a median of nearly nine months increase in progression free survival compared with patients taking standard therapy alone.

“We want to develop more effective approaches for patients with non-small cell lung cancer,” says co-principal investigator Pasi A. Jänne, MD, PhD, director of the Lowe Center for Thoracic Oncology at Dana-Farber. “One way to do that is to intensify the initial treatment we give.”

Jänne presented the findings at the International Association for the Study of Lung Cancer (IASLC) World Conference on Lung Cancer in Singapore on Monday, September 11.

About 10%-15% of patients in the U.S. and 50% of patients in Asia with NSCLC harbor EGFR mutations in their tumors. The mutation fuels the growth of the cancer.

These patients receive standard therapy of osimertinib [Tagrisso], a third generation EGFR-tyrosine kinase inhibitor (EGFR-TKI) that precisely targets and blocks the oncogenic mutation. Osimertinib has been shown to be more effective than previous generations of EGFR-TKIs.

However, patients can still develop resistance to the drug and relapse. One way to treat resistance is to wait for it to occur and treat the recurrence by adding chemotherapy.

“In this trial, we took a complementary approach and added the chemotherapy up-front to determine if it would stave off resistance,” says Jänne.

Evidence from previous studies had shown that earlier generation EGFR-TKIs plus chemotherapy

had improved efficacy, suggesting that the strategy of intensifying initial therapy had merit.

After an initial test of the safety of the combination of osimertinib and chemotherapy, this trial randomized 557 patients with EGFR-mutated advanced NSCLC to receive either osimertinib alone or osimertinib in combination with pemetrexed plus either cisplatin or carboplatin chemotherapy. Patients randomized to receive the combination had four treatments of chemotherapy over the course of three months and then continued with osimertinib plus pemetrexed.

The median progression-free survival for patients taking the combination was 25.5 months versus 16.7 months for those taking osimertinib alone. Patients receiving the combination experience more adverse events associated with the added chemotherapy.

“It was a significant improvement in progression-free survival,” says Jänne. “While we don’t know if that translates to an improvement in Overall Survival, osi + chemo provided significant benefit for all patients in the trial.”

The study is still ongoing. The investigators will continue to observe patients to determine if overall survival is improved with the more intense therapy. They also will analyze the data, blood samples, and tumor biopsies they’ve collected to determine if there are subsets of patients who are more likely to respond to the combination therapy.

“Some patients already do very well for an extended time on osimertinib alone,” says Jänne. “If we have a better sense of who needs the added chemotherapy, we can convey that to patients and discuss the risks and benefits.”

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