# 分子標的治療は肺がんの再発を遅延させる (Abstract 8500)

## ADJUVANT：ゲフィチニブは非小細胞肺がんの再発予防において術後補助化学療法よりも有効である

## ADJUVANT: Gefitinib more effective than adjuvant chemotherapy in preventing recurrence of non-small cell lung cancer

分子標的治療薬ゲフィチニブは、標準治療である化学療法よりも術後再発予防においてより有効なようである。第III相臨床試験において、ゲフィチニブを投与された上皮成長因子受容体（*EGFR*）陽性、ステージII-IIIA非小細胞肺がん（NSCLC）の患者は、通常の化学療法を受けた患者に比べ、無再発期間が約10か月長かった。再発までの期間中央値は、ゲフィチニブ群で28.7か月であり、化学療法群で18か月であった。試験期間中に76人が死亡した（全登録患者の34.2%）；41人はゲフィチニブ群、35人は化学療法群であった。このスタディ結果は2017年American Society of Clinical Oncology年次集会で発表された。

## Full Text

The targeted therapy gefitinib appears more effective in preventing recurrence after lung cancer surgery than the standard of care, chemotherapy. In a phase III clinical trial, patients with epidermal growth factor receptor (*EGFR*)-positive, stage II-IIIA non-small cell lung cancer (NSCLC) who received gefitinib went about 10 months longer without recurrence than patients who received chemotherapy. The study is being presented at the 2017 ASCO Annual Meeting.

"Adjuvant gefitinib may ultimately be considered as an important option for stage II-IIIA lung cancer patients with an active *EGFR* mutation, and we may consider routine *EGFR* testing in this earlier stage of lung cancer," said lead study author Yi-Long Wu, MD, a director of the Guangdong Lung Cancer Institute, Guangdong General Hospital, Guangzhou, China. "We intend to follow these patients until we can fully measure overall survival as opposed to disease-free survival, which just measures disease recurrence."

Due to high chance of recurrence, the five-year survival for patients with stage II-IIIA NSCLC is only 40%. About 25% of all patients who are diagnosed with NSCLC are eligible to have surgery to remove the tumors with the hope of a cure. Among that group, about 30% or 140,000 people worldwide have an *EGFR* mutation in the tumor and may benefit from adjuvant treatment with *EGFR*-targeted therapy to reduce the chance of recurrence.

Following surgery, 222 patients who had confirmed activating *EGFR* mutations in the tumor were randomly assigned to receive gefitinib or chemotherapy (vinorelbine plus cisplatin). Patients received gefitinib daily for 24 months or the standard therapy regimen every three weeks for four cycles. According to the authors, chemotherapy was given for a shorter period of time because it is usually not tolerated well for longer periods of time. All patients were followed for disease relapse for about three years.

"Two recent targeted therapy trials of adjuvant therapy did not show benefit in NSCLC, in part because they included stages I, II, and III of the disease in their design," said Dr. Wu. "The earlier trials only looked to see if patients showed overexpression, or over-activity, of *EGFR*, but not mutations in *EGFR*. Our trial recruited patients who had been confirmed to have activating *EGFR* mutations so we believe these reasons account for why other trials showed no benefit of a targeted therapy while ours did."

Gefitinib blocks the signaling through the *EGFR* and is only effective in cancers with mutated and overactive *EGFR*.

The median time to recurrence was 28.7 months for patients who received gefitinib and 18 months for those who received chemotherapy. There were 76 patient deaths (34.2% of all enrollees) during the trial period; 41 occurred in the gefitinib group and 35 in the chemotherapy group.

Far fewer patients experienced severe side effects with gefitinib (12%) than with chemotherapy (48%). The most common serious side effect in the gefitinib group was elevated liver enzymes, whereas patients in the chemotherapy group had more severe quality of life concerns, including vomiting, nausea, low blood counts, and anemia.

As the researchers have a tissue repository from the surgically removed lung tumors, they plan to perform a comprehensive biomarker analysis looking for other potential biomarkers for gefitinib response or resistance, in addition to *EGFR*. Dr. Wu stated that a fuller analysis of treatment outcomes is also planned.

"This study identifies a subset of patients with lung cancer who can benefit from a targeted treatment that causes far fewer side effects than chemotherapy," said ASCO President-Elect Bruce E. Johnson, MD, FASCO. "It's also clear evidence that we can use precision medicine not only in patients with advanced cancer, but also in those with earlier stage disease."

ADJUVANT (NCT01405079) is the first randomized trial to compare gefitinib (G) with vinorelbine+cisplatin (VP) in completely resected pathological stage II-IIIA (N1-N2) NSCLC with *EGFR*-activating mutation.

This study received funding from Chinese Thoracic Oncology Group (CTONG) and AstraZeneca China.

## ASCO2017特集