Adjuvant chemotherapy in stage I lung cancer: Is more better?

Chuong D. Hoang, MD

From the Section of Thoracic Surgery, National Cancer Institute-National Institutes of Health, Center for Cancer Research, and The Clinical Center, Bethesda, Md.

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Address for reprints: Chuong D. Hoang, MD, Section of Thoracic Surgery, National Cancer Institute-National Institutes of Health, Center for Cancer Research, and The Clinical Center, 10 Center Dr, Mail Code 1201, Room 4-3940, Bethesda, MD 20892 (E-mail: chuong.hoang@nih.gov).

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Central Message

Indications for adjuvant chemotherapy in resected lung cancer may evolve with ongoing refinements in the TNM staging system, particularly with greater appreciation of high-risk tumor features.

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With the new eighth edition TNM staging system for non-small cell lung cancer (NSCLC), there is better stratification, particularly in early stages, based on objective analyses revealing distinct survival differences according to tumor size in increments of 1 cm (up to 5 cm). Now, an opportunity exists to re-examine standard-of-care practices for NSCLC based on new definitions of TNM stage.

Despite resection of NSCLC, the 5-year overall survival (OS) varies from 90% in patients with pathologic stage IA1 to 41% in those with stage IIIA.¹ The majority of patients with NSCLC are offered adjuvant chemotherapy based on phase III trials (reported between 2003 and 2006) that, when meta-analyzed in 2008,² demonstrated survival benefit for patients with stage II to IIIA disease and a likely detrimental effect in patients with stage IA disease.

The clinical approach to stage IB disease remains controversial because of confounding results. The mature reporting of Cancer and Leukemia Group B 9633,³ the only randomized trial specifically investigating adjuvant chemotherapy in patients with stage IB disease, indicated no OS benefit. However, an updated meta-analysis of more than 4500 patients pooled from 16 trials with resected stage IB disease showed that adjuvant chemotherapy associated with a significant OS improvement (hazard ratio, 0.74; 95% confidence interval, 0.63-0.88; $P < .001$).⁴ The benefit was realized mostly in those patients receiving uracil and tegafur (not approved for use in the United States), whereas there was no benefit associated with platinum-based chemotherapy. Lastly, a recent multivariate analysis of the National Cancer Data Base (2004-2011) revealed improved median and 5-year OS in patients with resected NSCLC tumors 3.1 to 3.9 cm in size, among other sizes comprising T2 (seventh edition TNM), who received adjuvant chemotherapy (hazard ratio, 0.77; 95% confidence interval, 0.70-0.83; $P < .001$).⁵

Following this modern trend suggesting that adjuvant chemotherapy may be beneficial in smaller NSCLC tumors, Wang and colleagues⁶ explore the intriguing notion of adjuvant chemotherapy in the subgroup of resected NSCLC patients with stage IA1 to IA3 and IB disease stratified by lymphovascular invasion status of the primary tumor. Their unique multidisciplinary, locoregional practice allowed adjuvant chemotherapy in patients with stage I disease, contrary to guidelines established earlier.² Certainly, the improved recurrence-free survival and OS rates in all stage I subgroups with lymphovascular invasion, as reported here, will inspire other, similar investigations. Thus, Wang and colleagues⁶ reopen the discussion on indications for adjuvant chemotherapy in resected NSCLC as well as inform about the design options of prospective trials in this area.

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