# Adjuvant Therapy Choices in Patients With Resected Non-Small-Cell Lung Cancer: Correlation of Doctors' Treatment Plans and Relevant Phase III Trial Data

*By Mark R. Green, MD, Michele Andrews, MPH, Richard Leff, MD, FACP, Joanne Willey, RN, Carmen Allegra, MD, Alex Denes, MD, FACP, James Epstein, MD, James Jones, MD, and Lee Lokey, MD*

Network for Medical Communications and Research, Atlanta, GA

## Abstract

**Purpose:** To evaluate case-based choices selected from among preselected options for adjuvant therapy management in patients with completely resected non-small-cell lung cancer (NSCLC).

**Methods:** In a series of meetings in which US oncologists participated in case-based discussions, market research data were acquired using audience response keypad technology. Participant's anonymous responses to specific case-based questions were recorded electronically and tabulated.

**Results:** Core behaviors among the majority of physician participants are driven by emerging level 1 evidence. However, a "more aggressive than literature-supported treatment posture" is frequently selected. For the scenario involving a patient with completely resected pT1N0 disease, approximately 60% recommended observation but one third of respondents indicated they would propose three to four cycles of platinum-based adjuvant chemotherapy. Twenty-three percent would recommend adjuvant radiation following adjuvant chemotherapy for a patient with completely resected pT2N1 (stage IIB) disease. In the stage IIB setting, when cisplatin or carboplatin chemotherapy choices were specified, carboplatin-based combinations were selected by 43.6% compared with 30% for cisplatin regimens. Eight respondents (3.5%) favored observation for the stage IIB setting. This is consistent with the preponderance of level 1 evidence for adjuvant management. Carboplatin combinations are also recommended despite the availability of only abstract data and a meeting report for a single phase III trial showing a survival benefit for carboplatin based management in stage IB disease. The use of radiation as an element in adjuvant therapy in the settings assessed in this research is not supported by prospective data.

**Conclusions:** Treatment plans that include adjuvant platinum-based chemotherapy have been widely adopted by US oncologists for a large fraction of patients with completely resected NSCLC. Recommendations for adjuvant chemotherapy for the patient described here with stage IA disease, or for adjuvant radiation alone or after adjuvant chemotherapy, for the stage IIB disease patient presented are overly aggressive, not evidence based, and carry potential harm. In settings in which level 1 evidence for a survival benefit from adjuvant chemotherapy does exist, some of the specific adjuvant chemotherapy regimens selected, while widely used in NSCLC patients with more advanced disease, have not yet been demonstrated to provide improved disease-free or overall survival as adjuvant treatment. Individualized adjuvant treatment recommendations not specifically grounded in level 1 evidence appear to be widely recommended by US medical oncologists for patients with completely resected NSCLC.

## Introduction

The potential for surgical cure in patients with solid tumors depends on many factors: the chance of discovering the primary tumor relatively early in its clinical history; the sensitivity and effective application of staging; the completeness of surgical resection, and the statistical likelihood of micrometastatic disease spread at the time of diagnosis.[1] Postsurgical adjuvant therapy is designed to reduce the risk of recurrence and improve overall survival. Optimum adjuvant strategies involve systemic therapy and may involve the addition of locoregional consolidation if they can be based on known patterns of failure in individual diseases and stages.

Adjuvant systemic therapy has been a worldwide standard for breast cancer patients for the past quarter century.[1] More recently, adjuvant therapies in patients with node-positive colon cancer and gastric cancer[2] have become routine. Use of adjuvant chemotherapy in lung cancer has lagged well behind these other common solid tumors because of absence of demonstrated survival benefit in phase III trials of adjuvant chemotherapy in non-small-cell lung cancer (NSCLC) patients. In 2003, Le Chevalier et al[3] presented the results of the first large phase III, trial to show a statistically significant survival benefit using traditional combination chemotherapy compared with no postsurgical treatment as management for patients with NSCLC.[4] The absolute survival improvement was 4.1% at 5 years for treatment versus observation (44.5% *v* 40.4%; $P = .03$). Some investigators considered this as proof of adjuvant efficacy while others were cautious about the clinical relevance of the findings. In June, 2004 two additional adjuvant therapy trials[5,6] were reported at the American Society of Clinical Oncology (ASCO) Annual Meeting in New Orleans. Each compared four cycles of a platinum-based chemotherapy regimen to postsurgical observation. In each trial, the reported survival benefit was highly statistically significant and the absolute survival difference of 12% to 15% was interpreted as very encouraging.

We were interested to know how oncology practitioners were using the evolving adjuvant therapy data in day-to-day

patient management. At four market research meetings spread over the course of 2004, we asked a total of 288 oncology physicians how they would treat hypothetical patients with specific stages of completely resected NSCLC. Their answers, presented in this article, suggest rapid application of the clinical data to individual patient care. However, the treatment options selected are not always fully supported by the available data and show the tendency of physicians to individualize their treatment approaches beyond the available evidence. Our findings have important implications for dissemination of new information to treating physicians and provide lessons about their application of such data to current practice.

## Methods

Physicians self-selected to participate in 1-day oncology market research meetings organized by the Network for Medical Communications and Research (NMCR). Meeting expenses, including participant travel costs and out-of-pocket expense reimbursement, were supported from revenues paid to NMCR by multiple pharmaceutical sponsors. Physician attendees were not provided honoraria. Market research data were acquired using audience response keypad technology. Anonymous participant responses to specific case-based questions were recorded electronically. Questions typically offered four to eight response choices and could include follow-up questions to probe one area in greater detail. After the question was presented by the meeting moderator and the anonymous answers of the attendees were entered and tallied, the results were immediately presented in bar graph form so that each attendee could see the different treatment options selected by the meeting participants. Following this acquisition and display of the response information, a recognized expert in the disease area under discussion would review the case and discuss the available data supporting each of the treatment options offered. Open discussion of the issues between the expert and the attendees, and among the attendees, followed.

Four meetings investigating issues in lung cancer therapy, including adjuvant management strategies, were organized by NMCR during 2004. Dates and sites are shown below.

**"CC Lung" 2004**
**4 meetings distributed through the year**

| | |
|---|---|
| • New Orleans | March 13 |
| • New York City | April 17 |
| • Boston | August 7 |
| • Miami | November 6 |

A total of 288 physicians attended and participated in generation of the research data. Not all participants provided a keypad response to each of the questions, but for each question the database responses included a majority of attendees. Two specific questions focused on use of adjuvant therapy strategies in completely resected NSCLC. The first involved a patient with stage IA disease while the second was based on a patient with a stage IIB tumor.[7] The specific wording of the questions and the treatment choices offered are shown in Table 1.

## Results

The first case presented a patient with stage IA disease. The tumor was less than 1 cm in diameter. Staging computed tomography (CT; anatomic imaging) and positron emission tomography (PET; physiologic imaging) studies did not suggest any spread of tumor. Surgical resection was accomplished with a lobectomy. Resection margins were

**Table 1. Specific questions focused on use of adjuvant therapy strategies in completely resected NSCLC**

### Question 1:

A 63 year old man with a 2 pack/day smoking history is entered in the National Lung Cancer Screening Trial. He has a low exposure helical CT scan which shows a 7mm nodule in the left lower lobe. A follow up formal diagnostic chest CT is negative for other abnormalities. A PET scan is also negative. The patient undergoes a thoracotomy, left lower lobectomy and sampling of nodal levels 5, 6, 7, 8, and 9. The primary is large cell carcinoma with the largest diameter of 0.8 cm and no pleural involvement. 0 of 13 nodes are positive for cancer. He is referred to you for a discussion of post operative therapy.

**What treatment would you recommend?**

1. 3-4 cycles of adjuvant cisplatin-based chemotherapy
2. 2 cycles of adjuvant cisplatin-based chemo followed by gefitinib for 1–2 years
3. 3-4 cycles of adjuvant carboplatin-based chemotherapy
4. 2 cycles of platinum-based chemotherapy
5. Gefitinib for 1-2 years
6. No post operative adjuvant therapy

### Question 2:

A 71 year old male with well-controlled hypertension on an ACE inhibitor presents to his internist with a new onset dry cough. PMH is significant for a CABG x 3 vessels 6 years ago, after which he stopped smoking. His internist orders a CXR which reveals a right suprahilar mass. Chest CT confirms a 4 cm medial RUL mass and suggests hilar adenopathy. The mediastinum appears normal. Bronchoscopy shows an endobronchial lesion and biopsy is positive for squamous cell carcinoma. PET scan is positive in the lung and right hilum only. Thoracotomy with right upper lobectomy confirm the 4.5 cm squamous cell carcinoma and 3/7 hilar nodes are positive. Level 2R, 4R, and level 7 nodes are negative for metastatic tumor. He recovers rapidly and he is referred to you for a discussion of post operative therapy.

**What treatment would you recommend?**

1. Observation
2. Adjuvant radiation of ~50 Gy in 5 weeks
3. 3-4 cycles of adjuvant paclitaxel and carboplatin
4. 3-4 cycles of adjuvant docetaxel and cisplatin
5. 3-4 cycles of adjuvant docetaxel and carboplatin
6. 3-4 cycles of adjuvant gemcitabine and cisplatin
7. 3-4 cycles of adjuvant gemcitabine and carboplatin
8. Adjuvant chemotherapy followed by radiation

negative. Intraoperative nodal staging included comprehensive assessment of relevant nodal stations. Postoperative management choices selected by attendees are shown in Table 2. Approximately 60% of respondents (127 of 210) indicated that they would observe this patient with no planned postoperative adjuvant management. Among the remaining physicians, five chose to recommend two cycles of adjuvant cisplatin-based chemotherapy and two selected the same chemotherapy followed by 2 years of adjuvant gefitinib (Iressa). Nearly 35% of participants said they would prescribe three to four cycles of platinum-based adjuvant chemotherapy. Among this latter group, a cisplatin combination was favored by almost 26% (54 of 210) compared with a carboplatin combination by 9% (19 of 210). When carboplatin usage was broken down by meeting date, it was selected by 6.8% of pre–ASCO Annual Meeting 2004 participants compared with 12% addressing the same question in the post–ASCO Annual Meeting period.

The second hypothetical patient had stage IIB disease. He was 74 years old and had significant comorbid illnesses.

**Table 2. Treatment recommendation selections by meeting**

| Meeting site | New Orleans | New York | Boston | Miami | Total |
|---|---|---|---|---|---|
| **Question 1** | | | | | |
| # respondents | 57 | 61 | 47 | 45 | 210 |
| Observe | 27 (47%) | 43 (70%) | 28 (60%) | 29 (64%) | 127 (60.5) |
| 2 cycles CT | 2 (4%) | 1 (2%) | 2 (4%) | 0 | 5 (2.4%) |
| 2 cycles CT Gefitnib ➡ | 0 | 1 (2%) | 0 | 1 (2%) | 2 (1.0%) |
| Gefitinib x 2 yrs | 0 | 2 (3%) | 0 | 1 (2%) | 3 (1.4%) |
| Cis doublet x 3-4 | 22 (29%) | 12 (20%) | 13 (28%) | 7 (16%) | 54 (25.7%) |
| Carbo doublet x 3-4 | 6 (11%) | 2 (3%) | 4 (9%) | 7 (16%) | 19 (9%) |
| **Question 2** | | | | | |
| # respondents | 55 | 65 | 66 | 43 | 229 |
| Observation | 3 (5%) | 3 (5%) | 1 (2%) | 1 (2%) | 8 (3.5%) |
| Radiation (TRT) | 2 (4%) | 0 | 0 | 0 | 2 (0.9%) |
| CT ➡ TRT | 15 (27%) | 16 (25%) | 15 (23%) | 6 (14%) | 52 (22.7%) |
| Cis doublet x 3-4 | 14 (25.5%) | 17 (26.2%) | 22 (34.4%) | 15 (34.9%) | 68 (29.7%) |
| Carbo doublet x 3-4 | 21 (38.2%) | 29 (44.6%) | 28 (43.8%) | 21 (48.8%) | 99 (43.2%) |

Nonetheless, he tolerated his staging and primary surgical therapy, a lobectomy, without incident. Intraoperative evaluation of right-sided N2 nodal stations did not reveal tumor. In this case, a large majority (95.6%) of the meeting participants indicated that they would recommend adjuvant combination chemotherapy. Almost 73% (165/227) selected three to four cycles of platinum-based doublet therapy. An additional 22.7% (52 of 227) said they would use adjuvant chemotherapy followed by radiation consolidation. Only two respondents (1%) suggested postoperative radiation without any chemotherapy, whereas eight (3.5%) favored observation as their preferred choice of management. Analyzing the treatment selections based on meetings before or after ASCO Annual Meeting 2004, no systemic therapy was selected by 6.7% of participants (8 of 120) in the two pre–ASCO Annual Meeting sessions compared with 2% (2 of 107) at the post–ASCO Annual Meeting sessions. Carboplatin based combinations were selected by 41.5% in the first two meetings compared with 45.7% in the 2 post–ASCO Annual Meeting sessions.

Combination chemotherapy adjuvant treatment options offered in the second patient reflected regimens routinely used by US oncologists in patients with stage IV NSCLC. They included either of two taxanes or the antimetabolite gemcitabine combined with a platinum salt. Etoposide or vinorelbine plus platinum options, infrequently used in American patients for first line management of stage IV disease, were not offered. In the aggregate, 68 physicians (30%) selected paclitaxel and carboplatin as their preferred adjuvant regimen. Docetaxel and cisplatin was chosen by 51 (22%) and docetaxel and carboplatin by 23 (10%). Gemcitabine regimens with cisplatin or carboplatin were chosen by 17 and eight physicians (7% and 3%), respectively. As reported earlier, 52 additional physicians (23%) said they would use adjuvant chemotherapy followed by radiation (Table 3).

## Discussion

Adjuvant chemotherapy is a widely used, evidence-based treatment approach in selected patients with breast and colorectal cancer. The magnitude of recurrence risk considered sufficient to

**Table 3. Platinum doublets selected in question 2**

| | Cisplatin | Carboplatin |
|---|---|---|
| Paclitaxel | N/A | 68 (30%) |
| Docetaxel | 51 (22%) | 23 (10%) |
| Gemcitabine | 17 (7%) | 8 (3%) |

warrant adjuvant therapy varies worldwide. However in the United States essentially all patients with node-positive breast and colon cancers and a large fraction of those with node-negative breast cancer are routinely considered adjuvant therapy candidates.[1, 2]

In 1995, an individual patient data based meta-analysis of the impact of adjuvant chemotherapy in patients with non-small-cell lung cancer was reported by a consortium of international investigators (Table 4).[10] In that report, the aggregate 5-year survival expectation among nearly 1,400 completely resected patients was approximately 50%. Compared with patients observed postoperatively, the hazard ratio for survival in the patients who received adjuvant chemotherapy was .87 and the log-rank $P_2$ value was .08. The findings were considered encouraging, consistent with a 5% survival benefit at 5 years; the intervention was not effective enough so that a positive result could also be attributed to a random occurrence at the $P$ = .05 level. Additional, larger trials with observation control arms were considered appropriate.

**Table 4. Recent phase III randomized therapy trials using 3 to 4 courses of adjuvant platinum based chemotherapy**

| Study | # Pts | Control | Adj Rx | 5 yr survival Cont | Rx | P |
|---|---|---|---|---|---|---|
| Meta-analysis[10] | 1394 | Observe | CT (any) | 50% | 55% | 0.08 |
| ECOG 3590[13] | 448 | TRT (Thoracic radiotherapy) | EP/TRT + EP | Not specifically reported | | 0.56 |
| ALPI[14] | 1209 | Obs ± TRT | MVP x 3 ± TRT | 47% | 52% | 0.58 |
| IALT[3,4] | 1867 | Obs ± TRT | CT (4 choices) x 3 to 4 cycles + TRT | 44.5% | 40.4% | 0.03 |
| JBR-10[5] | 482 | Observe | Vin-cis x 4 | 54% | 69% | 0.012 |
| CALGB 9633[6] | 344 | Observe | Pac-carbo x 4 | 71% | 59%* *4 yr survival data | 0.028 |

In 1998, a different meta-analysis, this time focusing on prospectively randomized adjuvant radiotherapy trials in resected NSCLC ("PORT Meta analysis") was reported by European investigators.[11,12] There was no survival benefit conveyed by postoperative radiation. In fact, in early-stage patients, there appeared to be a survival detriment. The work highlighted the fact that there was no prospective dataset showing a significant survival improvement for postoperative radiation therapy in NSCLC patients.

In the past 5 years, five individual trials [3-6,13,14] comparing no chemotherapy (control) to three to four courses of combination chemotherapy with or without sequential or concurrent radiation as adjuvant therapy for patients with resected NSCLC have been reported in manuscript or abstract form. The first of these trials, an Eastern Cooperative Oncology Group test of concurrent etoposide-cisplatin and radiation followed by additional chemotherapy compared with adjuvant radiation alone showed neither a disease-free nor overall survival advantage for the addition of chemotherapy.[13] Similarly, a large randomized Italian adjuvant chemotherapy trial (ALPI; Adjuvant Lung Project Italy) of mitomycin, vindesine and cisplatin with or without radiation consolidation failed to show a survival advantage for systemic therapy over observation (with or without radiation)[14]. These findings were the basis of the very common recommendation up until recently of observation only following complete resection in NSCLC patients.

Results of the International Adjuvant Lung Trial (IALT) were presented at the ASCO meeting in June 2003[3] and published 7 months later.[4] This was by far the largest adjuvant trial ever completed in NSCLC patients. Among the 1,867 patients on study, 36% had stage I (approximately 10% IA; 26% IB), 25% stage II, and 39% stage III. Random assignment to chemotherapy or no chemotherapy was prospectively stratified by pathologic stage. All chemotherapy options were cisplatin-based doublets given for three or four cycles. Fifty-six percent of patients randomly assigned to the chemotherapy arm were treated with etoposide-cisplatin, 27% received vinorelbine-cisplatin, 11% vinblastine-cisplatin, and 6 % vindesine-cisplatin. There was a statistically significant improvement in overall survival favoring chemotherapy ($P_2$ = .03) with a 4.1% absolute survival improvement. While there was no significant interaction between stage and efficacy, the manuscript figure showing benefits for adjuvant therapy by pathologic stage suggested a possible lesser benefit among the stage I patients than among those with more advanced stage.

Publication of the IALT ignited controversy among US oncologists. Thoracic surgeons, pulmonologists, primary care physicians, and the patients themselves were also aware of the controversy. Though the results suggested a benefit for cisplatin combinations, the impact of carboplatin-based adjuvant therapy was unknown. However, several North American adjuvant chemotherapy trials with random assignments including observation (no systemic therapy) control arms continued patient accrual.

In June 2004, two additional randomized, observation-controlled phase III trials of postoperative adjuvant therapy were reported. A study from the National Cancer Institute of Canada[5] in collaboration with US cooperative groups

enrolled 492 stage IB or II patients. The adjuvant chemotherapy prescription was vinorelbine at 25 mg/m$^2$ weekly x 16 doses with cisplatin given at 50 mg/m$^2$ days 1 and 8 every 4 weeks x four cycles. Five-year relapse-free survival rates were 61% and 48%, respectively, and 5-year overall survival figures were 69% and 54%, respectively ($P$ = 0.012). At the same meeting, early data from a US Intergroup experience in stage IB patients were also presented.[6] In that trial, 344 patients were randomly assigned to observation or four cycles of paclitaxel 200 mg/m2 and carboplatin (area under the curve, 6) administered every 3 weeks. The estimated 4-year survival for the treated patients was 71% compared with 59% among those assigned to observations ($P$ = .028).

The 1995 meta-analysis of adjuvant chemotherapy,[10] the PORT meta-analysis,[11,12] and the results of the first three of the five recent adjuvant therapy trials were the evidence base available to participants at the March and May 2004 market research meetings.[4,12-13] The results of both meta-analyses and all five recent phase III trials were available by the time the last two meetings in our 2004 the series took place.

In the first patient, with a less than 1-cm diameter primary tumor and no documented disease spread by radiographic and surgical staging, 60% of respondents recommended observation. This is consistent with the National Comprehensive Cancer Network (NCCN) guidelines for completely resected stage IA disease.[15] However, the remaining 40% selected use of a platinum-based chemotherapy regimen for two (3%) or three to four (35%) treatment cycles. Any use of adjuvant chemotherapy here is a very aggressive treatment recommendation given the patient's 5-year survival expectation of ≥ 90%[16] and the absence of specific data showing a statistically significant survival advantage for adjuvant chemotherapy in this subgroup. One large Japanese adjuvant therapy study of observation versus prolonged oral UFT adjuvant therapy also reported at ASCO Annual Meeting 2003[17] did show a survival advantage in the stage IB subset, but failed to show a survival benefit in stage IA patients.[18] None of the five prospective studies reported since 2000 had used just two cycles of chemotherapy, and there were no available data concerning the impact of adding of adjuvant gefitinib. However, these options were chosen by a few of the participants.

Similarly, prior to ASCO Annual Meeting 2004, there were no phase III randomized data demonstrating a survival benefit for any adjuvant carboplatin-based treatment approach. Yet, carboplatin doublet therapy was selected by 9% of respondents. Given that use of any chemotherapy in this setting is a very aggressive treatment posture, the choice of cisplatin over carboplatin by 75% of those who chose three to four cycles of adjuvant chemotherapy might be viewed as further pursuit of the most intensive treatment option offered.

The second patient, with stage IIB disease, falls squarely within the evidence base for the use of adjuvant chemotherapy.[3-6] Here over 90% of participants selected three to four cycles of adjuvant chemotherapy. Postoperative observation was chosen by nearly 7% of attendees in the first two meetings. This fell to 2% of respondents after the two adjuvant chemotherapy presentations at ASCO Annual Meeting 2004. In our hypothetical case, we chose to not offer the option of selecting a vinca alkaloid or topoisomerase II inhibitor in combination with a platinum agent as adjuvant therapy. These regimens are infrequently chosen for first line stage IV disease management in the United States. Since these were the specific chemotherapy combinations used in the IALT, the true meaningfulness of our observations about the specific chemotherapy regimens selected are somewhat compromised. However, several phase III trials in advanced disease have not revealed significant differences in terms of response and survival for vinorelbine or taxane, or gemcitabine plus platinum regimens. Thus, all the choices offered may be considered clinically relevant options.

Before ASCO Annual Meeting 2004, there were no reported data showing efficacy of carboplatin based adjuvant therapy in completely resected NSCLC patients. In addition at least one large randomized trial had shown a survival advantage in previously untreated patients with advanced NSCLC given paclitaxel cisplatin compared with paclitaxel carboplatin.[19] Yet, the respondents endorsed carboplatin-based adjuvant therapy options in just under half the patients with only a modest numerical increase between the pre– and post–ASCO Annual Meeting 2004 sessions. Whether this preference among US oncologists for better-tolerated therapy over potentially more-effective therapy will persist in the adjuvant setting, in which the goal is an increase in cure rates remains to be seen.

The option of adjuvant chemotherapy followed by radiation was selected by 23% of respondents. This approach in lung cancer patients is not currently supported by level 1 evidence (ie, evidence from properly conducted, controlled clinical trials).[4,11,12] This is especially true for the hypothetical stage IIB patient described in our question who did not have N2 (ipsilateral mediastinal) node involvement. With no evidence of augmented survival for postoperative radiation, this recommendation represents overly aggressive treatment with some potential for patient harm.[11]

These data reported here were acquired during four market research meetings held throughout 2004. They demonstrate that positive phase III results regarding adjuvant chemotherapy for lung cancer patients have been rapidly integrated into practice by US oncologists. However, where the lung adjuvant database is not specifically informative, many physicians appear willing to apply selected adjunctive strategies without level 1 evidence. In some cases overly aggressive management with postoperative radiation, essentially contraindicated by currently available information, is being recommended despite some

potential for harm. None of this is necessarily surprising in the US medicine paradigm, in which multiple considerations often converge. There may be a tendency among physicians to offer possibly useful treatment in the absence of evidence of statistically significant benefit. Individual assessments of the therapeutic index for a specific treatment approach can carry substantial weight. Patients and families often play an important role in these decisions, viewing an active intervention as "the best" or "only" strategy to "do everything" to keep the cancer from recurring. Other physician centric issues may also be involved. While additional randomized phase III trials of adjuvant therapy will be forthcoming, for at least the near future the kind of combined evidence—judgment decision matrix revealed by our research is likely to continue.

These methods of real-time, case-based, individual physician–centric, anonymous market research provide insights into the prescribing practices of selected US oncologists. We anticipate that these results can be at least somewhat generalized to the larger oncology practice base. We (and others[20]) are continuing to take the pulse of US oncologists relative to therapy choices for patients with several different malignancies. These additional observations will allow an extended longitudinal assessment of how medical oncology practitioners translate clinical research data to the care of individual patients.

## Authors' Disclosures of Potential Conflicts of Interest

Although all authors have completed the disclosure declaration, the following authors or their immediate family members have indicated a financial interest. No conflict exists for drugs or devices used in a study if they are not being evaluated as part of the investigation. Employment Relationship: Mark R. Green, Michele Andrews, Richard Leff, Joanne Willey, Carmen Allegra, Alex Denes, James Epstein, James Jones, Lee Lokey; Network for Medical Communications and Research. Consultant or Advisory Role: Mark R. Green, Sanofi-Aventis, Bristol-Myers Squibb, and Eli Lilly. Honoraria: Mark R. Green, Bristol-Myers Squibb, Eli Lilly, Sanofi-Aventis, Pfizer and GlaxoSmithKline. Stock ownership: Mark R. Green, Eli Lilly and Pfizer. Research Funding: Mark R. Green, GlaxoSmithKline. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section found in Information for Contributors at http://www.jopasco.org/

*Submitted April 21, 2005; accepted May 18, 2005*

*Corresponding author: Mark R. Green, MD, Medical Director, NMCR 780 Johnson Ferry Road, Suite 100, Atlanta, GA 30345, mgreen@nmcr.com*

## References

1. Fisher B: From Halsted to prevention and beyond: Advances in the management of breast cancer during the twentieth century. *Eur J Cancer* 35:1963-73, 1999
2. Macdonald JS: Clinical overview: Adjuvant therapy of gastrointestinal cancer. *Cancer Chemother Pharmacol* 54:S4-S11, 2004 (suppl 1)
3. Le Chevalier T for the IALT Investigators. Results of the Randomized International Adjuvant Lung Cancer Trial (IALT): Cisplatin-based chemotherapy (CT) vs no CT in 1867 patients (pts) with resected non-small cell lung cancer (NSCLC). *Proc Am Soc Clin Oncol* 22: A6, 2003
4. Arriagada R, Bergman B, Dunant A, et al: Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. *N Engl J Med* 350: 351-360, 2004
5. Winton TL, Livingston R, Johnson D, et al: A prospective randomized trial of adjuvant vinorelbine (VIN) and cisplatin (CIS) in completely resected stage 1B and II non small cell lung cancer (NSCLC) Intergroup JBR.10. *Proc Am Soc Clin Oncol* 23: A7018, 2004
6. Strauss GM, Herndon J, Maddaus MA, et al: Randomized clinical trial of adjuvant chemotherapy with paclitaxel and carboplatin following resection in Stage IB non-small cell lung cancer (NSCLC): Report of Cancer and Leukemia Group B (CALGB) Protocol 9633. *Proc Am Soc Clin Oncol* 23: A7018, 2004
7. Mountain CF: Revisions in the International System for Staging Lung Cancer. *Chest* 111:1710-1717, 1997
8. Vansteenkiste JF: FDG-PET for lymph node staging in NSCLC: A major step forward, but beware of the pitfalls. *Lung Cancer* 47:151-154, 2005
9. Feinstein AR, Sosin DM, Wells CK, et al: The Will Rogers phenomenon: Stage migration and new diagnostic techniques as a source of misleading statistics for survival in cancer. *N Engl J Med* 312:1604-1608,1985
10. Non-Small Cell Lung Cancer Collaborative Group. Chemotherapy in non-small cell lung cancer: A meta-analysis using updated data on individual patients from 52 randomized clinical trials. *BMJ* 311:899-909, 1995
11. PORT Meta-analysis Trialists Group: Postoperative radiotherapy in non-small-cell lung cancer: Systematic review and meta-analysis of individual patient data from nine randomized controlled trials. *Lancet* 352:257-263, 1998
12. Burdett S, Stewart L for the PORT Meta-Analysis Group: Post operative radiotherapy in non-small cell lung cancer: Update of an individual patient meta-analysis. *Lung Cancer* 47: 81-84, 2005
13. Keller SM, Adak S, Wagner H, et al: A randomized trial of postoperative adjuvant therapy in patients with completely resected stage II or IIIA non-small-cell lung cancer. *N Engl J Med* 343:1217-1222, 2000
14. Scagliotti GV, Fossati R, Torri V, et al: Randomized study of adjuvant chemotherapy for completely resected stage I, II, or IIIA non-small-cell lung cancer. *J Natl Cancer* Inst 95:1453-1461, 2003
15. NCCN guidelines for non-small cell lung cancer March, 2005. http://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf.
16. Bando T, Yamagihara K, Ohtake Y, et al: A new method of segmental resection for primary lung cancer: Intermediate results. *Eur J Cardiothorac Surg* 21: 894-899, 2002
17. Kato H, Tsuboi M, Ohta M, et al: A randomized phase III trial of adjuvant chemotherapy with UFT for completely resected pathological stage I (T1N0M0, T2N0M0) adenocarcinoma of the lung. *Proc Am Soc Clin Oncol* 22: A2498, 2003
18. Kato H, Ichinose Y, Ohta M, et al: Japan Lung Cancer Research Group on Postsurgical Adjuvant Chemotherapy: A randomized trial of adjuvant chemotherapy with uracil-tegafur for adenocarcinoma of the lung. *N Engl J Med* 350:1713-1721, 2004
19. Rosell R, Gatzemeier U, Betticher DC, et al: Phase III randomized trial comparing paclitaxel/carboplatin with paclitaxel/cisplatin in patients with advanced non-small-cell lung cancer: A cooperative multinational trial. *Ann Oncol* 13: 1515-1517, 2002
20. Buzdar A, Macahilig C: How rapidly do oncologists respond to clinical trial data? *Oncologist* 10:15-21, 2005