LCU | 2009 VOL 6 | ISSUE 1

Lung Cancer™ UPDATE

Conversations with Oncology Investigators
Bridging the Gap between Research and Patient Care

EDITOR

Neil Love, MD

INTERVIEWS

Roy S Herbst, MD, PhD

Primo N Lara Jr, MD

Giuseppe Giaccone, MD, PhD

Naiyer A Rizvi, MD

CME Certified

Subscribe to Podcasts or download MP3s of this program at ResearchToPractice.com/LCU

Lung Cancer Update
A Continuing Medical Education Audio Series

OVERVIEW OF ACTIVITY

Lung cancer is the leading cause of cancer mortality in the United States in both men and women, resulting in more deaths than breast, prostate, colon and pancreatic cancer combined. Progress in the screening, prevention and treatment of this disease has been limited, and about 85 percent of patients who develop lung cancer will die from it. Traditional chemotherapy, surgery and radiation therapy have had a modest effect on patient outcomes. However, with the advent of biologic agents, recent improvements have been seen in time to progression and survival in lung cancer clinical trials. Published results from ongoing and completed studies lead to the continual emergence of novel therapeutic strategies and changes in the indications for existing treatments. In order to offer optimal patient care — including the option of clinical trial participation — the practicing clinician must be well informed of these advances. Featuring information on the latest research developments along with expert perspectives, this CME program is designed to assist medical oncologists, hematologists and hematology-oncology fellows with the formulation of up-to-date clinical management strategies for the care of patients with lung cancer.

LEARNING OBJECTIVES

- Utilize clinical characteristics and tumor biomarkers in treatment decision-making for patients with lung cancer.
- Formulate an evidence-based algorithm for the use of adjuvant chemotherapy in localized non-small cell lung cancer (NSCLC).
- Communicate the benefits and risks of induction chemotherapy and concurrent chemoradiation therapy when recommending treatment strategies to patients with Stage III NSCLC.
- Integrate emerging data on the combined use of cytotoxic and biologic agents when selecting therapy for the first-line and subsequent care of patients with advanced NSCLC.
- Identify patients with NSCLC who are most likely to benefit from treatment with EGFR tyrosine kinase inhibitors and monoclonal antibodies.
- Assess the scientific and therapeutic applications of neoadjuvant systemic therapy for patients with locally advanced NSCLC.
- Apply the results of recently reported Phase III trials to the care of patients with extensive-stage small cell lung cancer.
- Counsel appropriately selected patients with lung cancer about the availability of ongoing clinical trials in which they may be eligible to participate.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this educational activity for a maximum of 3 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

HOW TO USE THIS CME ACTIVITY

This CME activity contains both audio and print components. To receive credit, the participant should review the CME information, listen to the CDs and complete the Post-test and Educational Assessment and Credit Form located in the back of this monograph or on our website at **ResearchToPractice.com/LCU**. This monograph contains edited comments, clinical trial schemas, graphics and references that supplement the audio program. **ResearchToPractice.com/LCU** includes an easy-to-use, interactive version of this monograph with links to relevant full-text articles, abstracts, trial information and other web resources indicated here in **blue underlined text**.

This program is supported by educational grants from Bristol-Myers Squibb Company, Genentech BioOncology/OSI Oncology, ImClone Systems Incorporated and Sanofi-Aventis.

Last review date: February 2009; Release date: February 2009; Expiration date: February 2010

TABLE OF CONTENTS

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

FACULTY — **Prof Giaccone** and **Dr Rizvi** had no real or apparent conflicts of interest to disclose. The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process: **Dr Herbst** — Consulting Agreements: Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Eli Lilly and Company, Genentech BioOncology, Pfizer Inc, Sanofi-Aventis; Paid Research: Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech BioOncology, Sanofi-Aventis. **Dr Lara** — Advisory Committee: Bayer Pharmaceuticals Corporation, Eli Lilly and Company, Genentech BioOncology, Pfizer Inc, Wyeth; Consulting Agreements: Bayer Pharmaceuticals Corporation, Eisai Inc, Genentech BioOncology, GPC Biotech, Novartis Pharmaceuticals Corporation, Pfizer Inc, Wyeth; Paid Research: Millennium Pharmaceuticals Inc; Speakers Bureau: Bayer Pharmaceuticals Corporation, Genentech BioOncology, Pfizer Inc.

EDITOR — **Neil Love**: Dr Love is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: Abraxis BioScience, AstraZeneca Pharmaceuticals LP, Aureon Laboratories Inc, Bayer Pharmaceuticals Corporation/Onyx Pharmaceuticals Inc, Biogen Idec, Bristol-Myers Squibb Company, Celgene Corporation, Eisai Inc, Eli Lilly and Company, Genentech BioOncology, Genomic Health Inc, GlaxoSmithKline, ImClone Systems Incorporated, Merck and Company Inc, Millennium Pharmaceuticals Inc, Novartis Pharmaceuticals Corporation, Ortho Biotech Products LP, OSI Oncology, Pfizer Inc, Roche Laboratories Inc, Sanofi-Aventis, Synta Pharmaceuticals Corp and Wyeth.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no real or apparent conflicts of interest to disclose.

INTERVIEW

Roy S Herbst, MD, PhD

Dr Herbst is Professor of Medicine and Cancer Biology, Chief of the Section of Thoracic Medical Oncology and Co-Chairman of the Phase I Working Group in the Department of Thoracic/Head and Neck Medical Oncology and the Department of Cancer Biology at The University of Texas MD Anderson Cancer Center in Houston, Texas.

Tracks 1-18

Track 1 Heading toward personalized medicine in lung cancer

Track 2 Performing biopsies in patients with advanced lung cancer

Track 3 Evaluation of tumor biomarkers in lung cancer

Track 4 Heterogeneity in biomarkers within tumors and across the disease spectrum

Track 5 Iressa® Pan-ASia Study (IPASS): First-line gefitinib versus carboplatin/paclitaxel for never/oligosmokers with advanced adenocarcinoma of the lung

Track 6 Use of adjuvant tyrosine kinase inhibitors (TKIs) for patients with EGFR mutation-positive early lung cancer

Track 7 Increased EGFR gene copy number by FISH and outcome with cetuximab and chemotherapy in non-small cell lung cancer (NSCLC)

Track 8 Planned SWOG-S0819 trial: Carboplatin/paclitaxel with cetuximab in EGFR FISH-positive advanced NSCLC

Track 9 Expanding patient eligibility for treatment with bevacizumab in NSCLC

Track 10 Analysis of the risk-benefit ratio of chemotherapy with bevacizumab versus cetuximab for advanced NSCLC

Track 11 Combination therapy targeting VEGF and EGFR in NSCLC

Track 12 BETA: Improvement in progression-free survival with the addition of bevacizumab to erlotinib as second-line therapy for advanced NSCLC

Track 13 Identification of predictors of response to bevacizumab in lung cancer

Track 14 Improved time to progression with the multikinase inhibitor vandetanib compared to docetaxel in previously treated advanced NSCLC

Track 15 Tolerability and side effects of vandetanib

Track 16 ZODIAC: A Phase III study of docetaxel with or without vandetanib in locally advanced or metastatic NSCLC

Track 17 Assessment of EGFR and RAS mutations as predictors of response to vandetanib

Track 18 Assessment of the safety and tolerability of cediranib with etoposide and cisplatin as first-line therapy for extensive-stage or metastatic lung cancer

Select Excerpts from the Interview

Tracks 7-8

DR LOVE: What do we know about cetuximab in the treatment of advanced NSCLC and potential predictors of response?

DR HERBST: Cetuximab is certainly an active agent in a number of tumor types, specifically colon, head and neck and now lung cancer. The FLEX trial — evaluating cisplatin/vinorelbine with or without cetuximab — was positive, yet the hazard ratio for overall survival was only 0.87 (Pirker 2008; [2.3]). That's a benefit, but it's a small benefit. Clinicians have been using it in practice, especially for patients with squamous cell tumors who can't receive bevacizumab, and I also administer it in that setting.

We need to find a biomarker to predict response because similar to other EGFR inhibitors, cetuximab produces a skin rash, and it can be quite burdensome for patients coming in for weekly treatments. We published a paper in the *Journal of Clinical Oncology* on a SWOG study that evaluated cetuximab concurrent with versus after chemotherapy as front-line therapy for patients with advanced NSCLC (Hirsch 2008). Median survival for the concurrent and sequential arms was 11 months versus 10 months respectively, which indicates that cetuximab might have an effect with chemotherapy and after chemotherapy.

An important finding from this study was that when we examined EGFR gene amplification by FISH, we found the median survival was doubled for patients on the concurrent arm with FISH-positive disease (1.1). This suggests that the EGFR gene copy number by FISH may be a useful predictor of which patients will benefit from cetuximab.

1.1 Clinical Outcomes According to EGFR Gene Copy Number Detected by FISH in Patients with NSCLC Treated with Paclitaxel/Carboplatin and Concurrent or Sequential Cetuximab

	All patients		Concurrent arm		Sequential arm	
	FISH- (n = 31)	FISH+ (n = 45)	FISH- (n = 15)	FISH+ (n = 25)	FISH- (n = 16)	FISH+ (n = 20)
Overall response	26%	45%	27%	42%	25%	50%
Median PFS	3mo	6mo	3mo	5mo	3mo	6mo
HR for PFS (*p*-value)		0.45 (0.001)		0.45 (0.02)		0.46 (0.03)
Median OS	7mo	15mo	8mo	16mo	7mo	15mo
HR for OS (*p*-value)		0.58 0.046		0.43 (0.03)		0.83 (0.65)

FISH = fluorescent in situ hybridization; PFS = progression-free survival; HR = hazard ratio; OS = overall survival

SOURCE: Hirsch FR et al. *J Clin Oncol* 2008;26(20):3351-7. **Abstract**

Track 12

DR LOVE: What do we know about combining bevacizumab and erlotinib in advanced NSCLC?

DR HERBST: The idea of using a nonchemotherapy doublet like this is attractive for avoiding cytotoxicities, such as myelosuppression and neuropathy. A Phase II trial evaluating this combination showed it was easy to administer, had minimal toxicity and demonstrated some good activity (Herbst 2005, 2007).

In the Phase III BeTa trial, with approximately 640 patients, erlotinib/bevacizumab was compared to erlotinib/placebo. Unfortunately, BeTa did not meet its primary endpoint of overall survival. However, it did meet the endpoints of progression-free survival and overall response (1.2).

The good news is that the combination clearly has some activity — it simply wasn't enough to demonstrate an improvement in survival. However, we have to wonder whether we can show a survival benefit in any second-line lung cancer trials in which 30 or 40 percent of the patients receive subsequent therapy. Many of those subsequent agents are probably active. We may not be able to use survival as our endpoint with these targeted agents.

1.2

Efficacy Data from the BeTa Trial: Second-Line Erlotinib (E) with or without Bevacizumab (B) in Advanced NSCLC

	Erlotinib + bevacizumab	Erlotinib + placebo	*p*-value	Hazard ratio (95% CI)
Median OS	9.3mo	9.2mo	0.75	0.97 (0.80-1.18)
Median PFS	3.4mo	1.7mo	<0.0001	0.62 (0.52-0.75)
ORR	12.6%	6.2%	0.006	NR

CI = confidence interval; OS = overall survival; PFS = progression-free survival; ORR = overall response rate; NR = not reported

SOURCE: Hainsworth J, Herbst R. *J Thorac Oncol* 2008;3(11 Suppl 4);**LBA1**.

Track 14

DR LOVE: Can you discuss the trial evaluating docetaxel with or without vandetanib?

DR HERBST: Vandetanib is an oral, multitargeted tyrosine kinase inhibitor (TKI). In a pilot trial, docetaxel/vandetanib was compared to docetaxel/placebo in a randomized Phase II design for patients previously treated for NSCLC. Two doses of vandetanib were evaluated — 100 milligrams versus 300 milligrams — and the endpoint of the trial was time to disease progression. Interestingly, time to progression improved from 12 to 18 weeks for

the patients who received the lower dose, whereas with the higher dose it improved but not significantly (1.3).

What does this mean? We know that EGFR inhibitors with chemotherapy are generally not effective in unselected patients. They might even inhibit the activity of chemotherapy. Many of us believe that at 100 milligrams, vandetanib is a good VEGF inhibitor, but it probably doesn't have much activity against EGFR. I believe 100 milligrams of vandetanib works as a good VEGF oral TKI — I believe it's one of the better ones. ■

1.3 **Phase II Study of Docetaxel with or without Vandetanib in Previously Treated NSCLC**

	Docetaxel + placebo (n = 41)	Docetaxel + vandetanib 100 mg (n = 42)	Docetaxel + vandetanib 300 mg (n = 44)
Median PFS	12.0wk	18.7wk	17.0wk
Hazard ratio (95% CI)	NA	0.64 (0.38-1.05)	0.83 (0.50-1.36)
p-value (two-sided)	NA	0.074	0.461

PFS = progression-free survival; CI = confidence interval

SOURCE: Heymach JV et al. *J Clin Oncol* 2007;25(27):4270-7. **Abstract**

SELECT PUBLICATIONS

Hainsworth J, Herbst R. **A Phase III, multicenter, placebo-controlled, double-blind, randomized clinical trial to evaluate the efficacy of bevacizumab (Avastin®) in combination with erlotinib (Tarceva®) compared with erlotinib alone for treatment of advanced non-small cell lung cancer after failure of standard first-line chemotherapy (BETA).** *J Thorac Oncol* 2008;3(11 Suppl 4);**LBA1**.

Herbst RS et al. **Phase II study of efficacy and safety of bevacizumab in combination with chemotherapy or erlotinib compared with chemotherapy alone for treatment of recurrent or refractory non small-cell lung cancer.** *J Clin Oncol* 2007;25(30):4743-50. **Abstract**

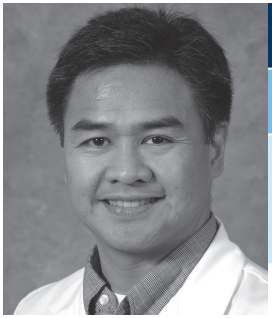
Herbst RS et al. **Phase I/II trial evaluating the anti-vascular endothelial growth factor monoclonal antibody bevacizumab in combination with the HER-1/epidermal growth factor receptor tyrosine kinase inhibitor erlotinib for patients with recurrent non-small-cell lung cancer.** *J Clin Oncol* 2005;23(11):2544-55. **Abstract**

Heymach JV et al. **Randomized, placebo-controlled phase II study of vandetanib plus docetaxel in previously treated non small-cell lung cancer.** *J Clin Oncol* 2007;25(27):4270-7. **Abstract**

Hirsch FR et al. **Increased EGFR gene copy number detected by fluorescent in situ hybridization predicts outcome in non-small-cell lung cancer patients treated with cetuximab and chemotherapy.** *J Clin Oncol* 2008;26(20):3351-7. **Abstract**

O'Neil BH et al. **High incidence of cetuximab-related infusion reactions in Tennessee and North Carolina and the association with atopic history.** *J Clin Oncol* 2007;25(24):3644-8. **Abstract**

Pirker R et al. **FLEX: A randomized, multicenter, phase III study of cetuximab in combination with cisplatin/vinorelbine (CV) versus CV alone in the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC).** *Proc ASCO* 2008;**Abstract 3**.



INTERVIEW

Primo N Lara Jr, MD

Dr Lara is Professor of Medicine and Associate Director of Translational Research at the University of California Davis Cancer Center in Sacramento, California.

Tracks 1-14

Select Excerpts from the Interview

Track 9

DR LOVE: Would you discuss your trial of intermittent erlotinib combined with pemetrexed (Davies 2008; [2.1])?

DR LARA: Four large randomized trials of chemotherapy with or without an EGFR TKI have demonstrated absolutely no benefit with the combination of

chemotherapy and either erlotinib or gefitinib (Herbst 2005, 2004; Gatzemeier 2007; Giaccone 2004). So at UC Davis, we have hypothesized that perhaps we can combine these agents with chemotherapy if they are administered intermittently according to a pharmacodynamic separation strategy. We've piloted the concept with docetaxel and, more recently, pemetrexed (2.1), but we need continued research to validate these observations.

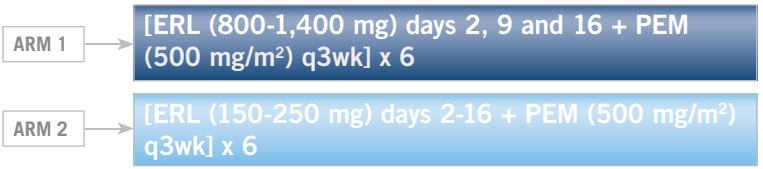
The results have been remarkable. The combination of docetaxel and erlotinib appears to improve, at least based on historical controls, the progression-free survival and overall survival of patients in the second-line setting (Davies 2007). Currently I'm chairing SWOG-S0709, in which we are treating patients with single-agent erlotinib or paclitaxel/carboplatin and erlotinib, administered with pharmacodynamic separation.

2.1

Intermittent Erlotinib (ERL) with Pemetrexed (PEM): Phase I Schedules Designed to Achieve Pharmacodynamic Separation

Protocol IDs: UCDCC-159, UCDCC-200412741-2, NCT00387322
Accrual: 42 (Closed)

Eligibility: Advanced tumors with no standard effective therapy available; Stage IIIB/IV NSCLC that progressed after platinum-based therapy or Stage IIIA/B NSCLC that progressed or recurred after first-line therapy



SOURCES: Davies AM et al. *Proc ASCO* 2008;Abstract 8032; www.clinicaltrials.gov.

Track 10

DR LOVE: What's your take on the Iressa® Pan ASia Study (IPASS) data presented by Tony Mok?

DR LARA: In IPASS, East Asian patients with advanced NSCLC were randomly assigned to receive either gefitinib or carboplatin/paclitaxel as first-line therapy. IPASS was unique in that the trial enrolled only patients with adenocarcinomas who were never smokers or past light smokers (<100 cigarettes in their lifetime). The group of patients was highly selected for the likelihood of possessing an EGFR mutation. It was a large trial with 600 patients in each arm. The hazard ratio for progression-free survival was 0.74 with a highly statistically significant *p*-value. A 26 percent reduction in the risk of progression was observed in favor of gefitinib (Mok 2008; [2.2]).

Not surprisingly, because the patients were mostly East Asian women with adenocarcinomas who were never smokers, EGFR mutations were found in

59 percent of the patients who provided samples. The patients who had EGFR mutation-positive disease appeared to benefit from first-line therapy with gefitinib compared to chemotherapy. In that population, the hazard ratio for progression-free survival was 0.48, which is remarkable (Mok 2008; [2.2]).

In contrast, the patients with EGFR mutation-negative disease — even though they were mostly women, East Asian and never smokers — did not benefit from gefitinib. In that particular subset, chemotherapy was the winner with a hazard ratio of 2.85 that was highly statistically significant (Mok 2008; [2.2]).

2.2

IPASS: A Phase III Randomized Trial of Gefitinib versus Carboplatin/Paclitaxel as First-Line Therapy for Clinically Selected* Patients with Advanced NSCLC

	Gefitinib	Carboplatin + paclitaxel	Hazard ratio (95% CI)	*p*-value
Progression-free survival events				
Intent-to-treat population (n = 609; 608)	74.4%	81.7%	0.74 (0.65-0.84)	<0.0001
EGFR mutation-positive (n = 132; 129)	73.5%	86.0%	0.48 (0.36-0.64)	<0.0001
EGFR mutation-negative (n = 91; 85)	96.7%	82.4%	2.85 (2.05-3.98)	<0.0001

* Asian patients with adenocarcinomas who were never smokers or past light smokers

CI = confidence interval

SOURCE: Mok T et al. *Proc ESMO* 2008;**LBA2**.

Track 12

DR LOVE: What are your thoughts about the FLEX trial?

DR LARA: This large Phase III trial of cisplatin/vinorelbine with or without cetuximab was the first test of whether cetuximab could improve outcomes for patients with NSCLC. Cetuximab did indeed improve outcomes, but the hazard ratio for overall survival was 0.87, which was marginal and modest at best. The median overall survival was even more modest, with barely a month difference (Pirker 2008; [2.3]).

I believe the FLEX trial confirms that cetuximab has clinical activity in advanced NSCLC. However, my enthusiasm for cetuximab with chemotherapy is somewhat dampened. First, the overall survival benefit was admittedly modest for the general population. Second, in the cetuximab arm, the rate of febrile neutropenia exceeded 20 percent (Pirker 2008) and bordered on an unacceptable range.

Third, one must factor in the inconvenience of weekly therapy with intravenous cetuximab, which is a challenge for many patients. I'm also a little wary about why the trial was positive for overall survival but demonstrated no

difference in progression-free survival (Pirker 2008; [2.3]). A fifth point that dampens my enthusiasm is the high cost of adding cetuximab to chemotherapy for a modest survival benefit. At some point, we as a society need to evaluate whether we can afford this. ■

2.3

FLEX: A Phase III Randomized Trial of Cisplatin/Vinorelbine (CV) with or without Cetuximab as First-Line Therapy for Patients with EGFR-Expressing Advanced NSCLC

Efficacy	CV + cetuximab (n = 557)	CV (n = 568)	Hazard ratio (95% CI)	*p*-value
Median overall survival				
All patients	11.3mo	10.1mo	0.871 (0.762-0.996)	0.044
Caucasians	10.5mo	9.1mo		
Asians	17.6mo	20.4mo		
Progression-free survival	4.8mo	4.8mo	0.943 (0.825-1.077)	NS
Time to treatment failure	4.2mo	3.7mo	0.860 (0.761-0.971)	0.015
Overall response rate	36%	29%	—	0.012

CI = confidence interval; NS = not significant

SOURCE: Pirker R et al. *Proc ASCO* 2008;**Abstract 3**.

SELECT PUBLICATIONS

Davies AM et al. **Intermittent erlotinib (ERL) in combination with pemetrexed (PEM): Phase I schedules designed to achieve pharmacodynamic separation.** *Proc ASCO* 2008;**Abstract 8032**.

Davies AM et al. **Pharmacodynamic separation of erlotinib and docetaxel (DOC) in advanced non-small cell lung cancer (NSCLC): Overcoming hypothesized antagonism.** *Proc ASCO* 2007;**Abstract 7618**.

Gatzemeier U et al. **Phase III study of erlotinib in combination with cisplatin and gemcitabine in advanced non-small-cell lung cancer: The Tarceva Lung Cancer Investigation Trial.** *J Clin Oncol* 2007;25(12):1545-52. **Abstract**

Giaccone G et al. **Gefitinib in combination with gemcitabine and cisplatin in advanced non-small-cell lung cancer: A phase III trial — INTACT 1.** *J Clin Oncol* 2004;22(5):777-84. **Abstract**

Herbst RS et al; TRIBUTE Investigator Group. **TRIBUTE: A phase III trial of erlotinib hydrochloride (OSI-774) combined with carboplatin and paclitaxel chemotherapy in advanced non-small-cell lung cancer.** *J Clin Oncol* 2005;23(25):5892-9. **Abstract**

Herbst RS et al. **Gefitinib in combination with paclitaxel and carboplatin in advanced non-small-cell lung cancer: A phase III trial — INTACT 2.** *J Clin Oncol* 2004;22(5):785-94. **Abstract**

Mok T et al. **Phase III, randomised, open-label, first-line study of gefitinib (G) vs carboplatin/paclitaxel (C/P) in clinically selected patients (pts) with advanced non-small-cell lung cancer (NSCLC) (IPASS).** *Proc ESMO* 2008;**LBA2**.

Pirker R et al. **FLEX: A randomized, multicenter, phase III study of cetuximab in combination with cisplatin/vinorelbine (CV) versus CV alone in the first-line treatment of patients with advanced non-small cell lung cancer (NSCLC).** *Proc ASCO* 2008;**Abstract 3**.

INTERVIEW

Giuseppe Giaccone, MD, PhD

Prof Giaccone is a medical oncologist in Bethesda, Maryland.

Tracks 1-12

Track 1	Immunotherapy for lung cancer
Track 2	Prevalence of EGFR mutations in Asians, and benefit from gefitinib compared to carboplatin/paclitaxel in the IPASS trial
Track 3	Role of EGFR mutation status, FISH amplification and clinical characteristics in the selection of patients enriched for response to erlotinib
Track 4	Incidence of EGFR TKI-associated interstitial pneumonitis in Asian patients
Track 5	Use of adjuvant erlotinib off protocol for patients with EGFR mutations
Track 6	Correlation between skin rash and antitumor activity of EGFR TKIs
Track 7	Erlotinib dose escalation in smokers and patients with CNS metastases
Track 8	Perspective on the FLEX trial results with cisplatin/vinorelbine and cetuximab for advanced, EGFR-overexpressing NSCLC
Track 9	Use of cetuximab with chemoradiation therapy for locally advanced NSCLC
Track 10	Predictors of bevacizumab-associated hemoptysis
Track 11	ECOG-E1505 and potential mechanisms of action of bevacizumab in the adjuvant setting
Track 12	Potential role for the multikinase TKIs, including vandetanib, in NSCLC

Select Excerpts from the Interview

Track 3

DR LOVE: What do we know about predictors of response to erlotinib?

PROF GIACCONE: Two major schools of thought exist regarding this topic. One advocates looking for EGFR mutations, and the other advocates determining the EGFR gene copy number by FISH.

It appears that FISH amplification can predict nonprogression, meaning tumor response or prolonged disease stabilization. It may be the easier way to select patients, especially in the western world, where at least 40 percent of the patients benefit from these drugs but mutations are not so frequent.

In the East, investigators have conducted studies in which they found FISH to be a useless predictor (Sone 2007). There, the incidence of EGFR mutations

is much higher, so the presence of mutation trumps FISH and immunohistochemistry. I expect that EGFR mutations will remain a powerful tool for selecting patients who will have major responses, and for the remainder of patients, FISH may be the better test (3.1).

In colon cancer, the presence of K-ras mutations is already used to select patients who should not receive cetuximab or panitumumab, and data are forthcoming in lung cancer with these mutations and the impact of TKIs, to which the presence of a K-ras mutation essentially predicts for no response (3.1) — and usually quick disease progression and a poor prognosis.

DR LOVE: In which populations do you feel the EGFR TKIs are appropriate to use off study?

PROF GIACCONE: Many centers are already treating patients who are never smokers with these agents in the front-line setting. Of course, the presence of EGFR mutations makes that argument even stronger. Now with the IPASS data, which showed a doubling of progression-free survival with gefitinib versus carboplatin/paclitaxel for never smokers and oligosmokers with advanced, EGFR mutation-positive adenocarcinomas, I expect many more will be doing so (Mok 2008).

The selection of therapy will not only be based on clinical factors, but it will also be supported by biomarkers and biological data.

3.1

Role of EGFR Genotypes and K-ras as Biomarkers of Response to Erlotinib: Analysis of NCIC BR.21

"We reported previously that, in BR.21, patients whose tumors expressed EGFR protein by immunohistochemistry and patients whose tumors had high *EGFR* copy number by FISH derived significant survival benefits from erlotinib compared with placebo. Patients with wild-type or *EGFR* mutations derived survival benefit from treatment, although the differences in survival compared with placebo were not significant. With analyses of additional samples that became available after our original report and a reanalysis of available samples for *EGFR* mutation by more sensitive techniques, the previous roles of *EGFR* mutation status and copy number were confirmed. We also report here that patients whose tumors have *KRAS* codon 12 and 13 mutations do not seem to derive any survival benefit from erlotinib therapy."

SOURCE: Zhu CQ et al. *J Clin Oncol* 2008;26(26):4268-75. **Abstract**

Track 5

DR LOVE: Are there any scenarios in which you would be willing to use adjuvant erlotinib for patients in your practice with EGFR mutations?

PROF GIACCONE: Although I believe chemotherapy is still the standard in the adjuvant setting, the field is changing rapidly. For a patient with Stage IIIA disease — extremely high risk — I would propose chemotherapy followed

by erlotinib. In earlier stages of disease in which the role of chemotherapy is doubtful, for example, in Stage IB disease, one might consider single-agent erlotinib. It should work because the mutations are sensitive to these drugs.

DR LOVE: For how long would you treat a patient with adjuvant erlotinib?

PROF GIACCONE: One year seems reasonable. No known cumulative toxicity exists with this agent, and side effects seem to lessen with time, essentially because of pharmacokinetic adaptation. ■

SELECT PUBLICATIONS

Besse B et al. **A phase II study of first-line erlotinib in patients (pts) with stage IIIB/IV non-small-cell lung cancer (NSCLC) including dose escalation to toxicity in current and former smokers (C/FS).** *Proc ASCO* 2008;**Abstract 8111**.

Eberhard DA et al; Non-Small-Cell Lung Cancer Working Group. **Biomarkers of response to epidermal growth factor receptor inhibitors in Non-Small-Cell Lung Cancer Working Group: Standardization for use in the clinical trial setting.** *J Clin Oncol* 2008;26(6):983-94. **Abstract**

Florescu M et al; National Cancer Institute of Canada Clinical Trials Group. **A clinical prognostic index for patients treated with erlotinib in National Cancer Institute of Canada Clinical Trials Group study BR.21.** *J Thorac Oncol* 2008;3(6):590-8. **Abstract**

Giaccone G et al. **Erlotinib for frontline treatment of advanced non-small cell lung cancer: A phase II study.** *Clin Cancer Res* 2006;12(20 Pt 1):6049-55. **Abstract**

Gounant V et al. **Subsequent brain metastasis responses to epidermal growth factor receptor tyrosine kinase inhibitors in a patient with non-small-cell lung cancer.** *Lung Cancer* 2007;58(3):425-8. **Abstract**

Hirsch FR et al. **Biomarker status correlates with clinical benefit: Phase 2 study of single-agent erlotinib (E) or E intercalated with carboplatin and paclitaxel (ECP) in an EGFR biomarker-selected NSCLC population.** *J Thorac Oncol* 2008;13(11 Suppl 4);**Abstract 11**.

Jackman DM et al. **Impact of EGFR and K-RAS genotype on outcomes in a clinical trial registry of NSCLC patients initially treated with erlotinib or gefitinib.** *Proc ASCO* 2008;**Abstract 8035**.

Mok TS et al. **The Phase III IRESSA™ Pan ASia Study (IPASS) compared efficacy, safety and tolerability of G with C/P in clinically selected chemonaïve pts with advanced NSCLC.** *J Thorac Oncol* 2008;13(11 Suppl 4);**LBA2**.

Popat S et al. **Recurrent responses to non-small cell lung cancer brain metastases with erlotinib.** *Lung Cancer* 2007;56(1):135-7. **Abstract**

Riely GJ et al. **Randomized phase II study of pulse erlotinib before or after carboplatin and paclitaxel in current or former smokers with advanced non-small-cell lung cancer.** *J Clin Oncol* 2009;27(2):264-70. **Abstract**

Sone T et al. **Comparative analysis of epidermal growth factor receptor mutations and gene amplification as predictors of gefitinib efficacy in Japanese patients with nonsmall cell lung cancer.** *Cancer* 2007;109(9):1836-44. **Abstract**

Wacker B et al. **Correlation between development of rash and efficacy in patients treated with the epidermal growth factor receptor tyrosine kinase inhibitor erlotinib in two large phase III studies.** *Clin Cancer Res* 2007;13(13):3913-21. **Abstract**

Wakelee H et al. **Optimal adjuvant therapy for non-small cell lung cancer — How to handle Stage I disease.** *Oncologist* 2007;12(3):331-7. **Abstract**

Zhu Chang-Qi et al. **Role of KRAS and EGFR as biomarkers of response to erlotinib in National Cancer Institute of Canada Clinical Trials Group study BR.21.** *J Clin Oncol* 2008;26(26):4268-75. **Abstract**

INTERVIEW

Naiyer A Rizvi, MD

Dr Rizvi is Associate Attending in Thoracic Oncology in the Department of Medicine at Memorial Sloan-Kettering Cancer Center in New York, New York.

Tracks 1-10

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: Would you discuss the role of neoadjuvant systemic therapy in NSCLC?

DR RIZVI: I believe that the use of neoadjuvant therapy is not completely accepted in this country, but it poses some advantages compared to adjuvant chemotherapy. First, one can determine whether the treatment works and shrinks the tumor. If it does, great, but if it does not, you can move on. Another advantage is that chemotherapy is difficult to administer after a big operation whereas we are better at administering drugs preoperatively. Across the board, only 60 to 70 percent of adjuvant chemotherapy can be delivered. Closer to 80 to 90 percent of preoperative chemotherapy, however, can be administered.

DR LOVE: Would you discuss your trials of preoperative therapy for NSCLC at Memorial Sloan-Kettering?

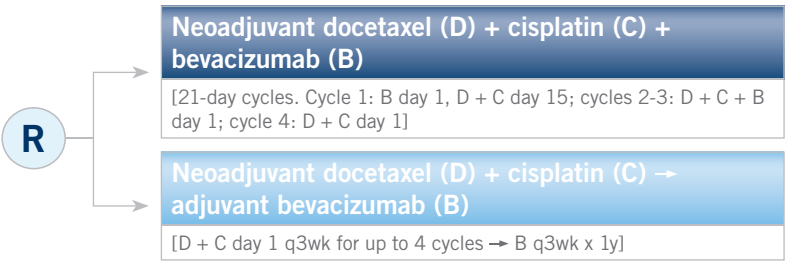
DR RIZVI: We are conducting two trials for patients with Stage IB to IIIA disease. One trial — BEACON (4.1) — is for patients whose tumors are less likely to have EGFR mutations. For patients with a significant smoking history, preoperatively we use four cycles of docetaxel/cisplatin and three cycles of bevacizumab.

So we leave a reasonable time frame between the last dose of bevacizumab and the time of surgery. Another group of patients in that trial will receive preoperative docetaxel/cisplatin followed by surgery and one year of adjuvant bevacizumab.

4.1

BEACON: A Phase II Study of Bevacizumab and Chemotherapy for Operable NSCLC

ID: 05-052
Enrollment: 70 (Open)



Primary Endpoint: Rate of pathologic downstaging
Secondary Endpoints: Overall survival, toxicity

Key Inclusion Criteria

- Stage IB, IIA, IIB or IIIA (T1-3N0-2M 0) NSCLC

Key Exclusion Criteria

- Prior treatment with chemotherapy, bevacizumab or radiation therapy
- Clinically significant cardiovascular disease
- Serious nonhealing wound, ulcer or bone fracture
- Prior malignancy in the past five years, other than nonmelanoma skin cancer and in situ carcinoma of the cervix

Stratification

- Patients with squamous cell carcinoma or nonsquamous cell large central tumor in proximity to blood vessels will be assigned to group B
- Patients with gross hemoptysis (defined as bright red blood of 1/2 teaspoon or more) within 28 days prior to treatment will now be allowed on protocol Arm B

Principal Investigator

Naiyer Rizvi, MD
Memorial Sloan-Kettering Cancer Center

SOURCE: www.clinicaltrials.gov.

We've been obtaining generally good results in terms of tumor regression and downstaging. We've also been able to perform these operations safely, without excess morbidity from preoperative bevacizumab. We've seen manageable hypertension and no other excess side effects. So the long-term maintenance-type approach with bevacizumab has been tolerated well.

We have another trial — ECON — for patients with a 15 pack-year or less smoking history. In that study, because of their minimal smoking history, we incorporate erlotinib into our treatment approach. The chemotherapy for that induction trial is pemetrexed/cisplatin.

Track 9

DR LOVE: Would you discuss the use of tumor histology in making treatment decisions?

DR RIZVI: Among patients with advanced NSCLC, the trial by Scagliotti comparing pemetrexed/cisplatin to gemcitabine/cisplatin as first-line therapy showed equivalence in terms of overall survival. However, patients with adenocarcinomas had a better chance of survival with pemetrexed/cisplatin, and patients with squamous cell histology had a better survival rate with gemcitabine/cisplatin (Scagliotti 2008; [4.2]).

Those are interesting data indicating that tumors with different histologies respond differently to chemotherapy. I do believe they're helpful data in terms of trying to tailor our treatment approach based on histology.

4.2

Randomized Phase III Trial of Cisplatin/Pemetrexed (CP) versus Cisplatin/Gemcitabine (CG) in Locally Advanced or Metastatic NSCLC

Endpoint	CP (n = 862)	CG (n = 863)	Adjusted HR (95% CI)
Median overall survival			
All histologic subtypes	10.3 months	10.3 months	0.94 (0.84-1.05)
Nonsquamous cell (n = 1,000)	11.8 months	10.4 months	0.81 (0.70-0.94)
Adenocarcinoma (n = 847)	12.6 months	10.9 months	0.84 (0.71-0.99)
Large cell carcinoma (n = 153)	10.4 months	6.7 months	0.67 (0.48-0.96)
Squamous cell (n = 473)	9.4 months	10.8 months	1.23 (1.00-1.51)

HR = hazard ratio; CI = confidence interval

SOURCE: Scagliotti GV et al. *J Clin Oncol* 2008;26(21):3543-51. **Abstract**

Track 10

DR LOVE: Would you discuss your trial with *nab* paclitaxel in Stage IV NSCLC?

DR RIZVI: *Nab* paclitaxel is nanoparticle albumin-bound paclitaxel and is free of Cremophor®, so no risk of hypersensitivity allergic reaction is associated with it. The study was an interesting trial for us because it was a front-line, single-agent trial for patients with Stage IV disease. The inherent bias for my colleagues and myself was to enroll patients who were older and had a lower performance status, because it was single-agent therapy. Nevertheless, single-agent *nab* paclitaxel on days one, eight and 15 of a 28-day schedule was quite active (Rizvi 2008; [4.3]). Aside from the neuropathy, it was well tolerated, and I believe it's a good regimen for patients. ■

4.3

Activity of Single-Agent *Nab* Paclitaxel as Initial Chemotherapy for Patients with Stage IV NSCLC

"A total of 40 patients were treated at 125 mg/m^2. The objective response rate was 30% (12 of 40 patients; 95% CI, 16% to 44%), median time to progression was 5 months (95% CI, 3 to 8 months), and median overall survival was 11 months (95% CI, 7 months to not reached). The 1-year survival was 41%...

NAB-paclitaxel 125 mg/m^2 administered on days 1, 8, and 15 of a 28-day cycle was well tolerated and demonstrated encouraging single-agent activity. No corticosteroid premedication was administered and no hypersensitivity reactions were seen."

SOURCE: Rizvi NA et al. *J Clin Oncol* 2008;26(4):639-43. **Abstract**

SELECT PUBLICATIONS

Albain KS et al. **Phase III study of concurrent chemotherapy and radiotherapy (CT/RT) vs CT/RT followed by surgical resection for stage IIIA(pN2) non-small cell lung cancer (NSCLC): Outcomes update of North American Intergroup 0139 (RTOG 9309).** *Proc ASCO* 2005;**Abstract 7014**.

Betticher DC. **Adjuvant and neoadjuvant chemotherapy in NSCLC: A paradigm shift.** *Lung Cancer* 2005;50(Suppl 2):9-16. **Abstract**

Gilligan D et al. **Preoperative chemotherapy in patients with resectable non-small cell lung cancer: Results of the MRC LU22/NVALT 2/EORTC 08012 multicentre randomised trial and update of systematic review.** *Lancet* 2007;369(9577):1929-37. **Abstract**

Green MR et al. **Abraxane, a novel Cremophor-free, albumin-bound particle form of paclitaxel for the treatment of advanced non-small-cell lung cancer.** *Ann Oncol* 2006;17(8):1263-8. **Abstract**

Hawkins MJ et al. **Protein nanoparticles as drug carriers in clinical medicine.** *Adv Drug Deliv Rev* 2008;60(8):876-85. **Abstract**

Kappers I et al. **Neoadjuvant (induction) erlotinib response in stage IIIA non-small-cell lung cancer.** *J Clin Oncol* 2008;26(25):4205-7. No abstract available

Rizvi NA et al. **Phase I/II trial of weekly intravenous 130-nm albumin-bound paclitaxel as initial chemotherapy in patients with stage IV non-small-cell lung cancer.** *J Clin Oncol* 2008;26(4):639-43. **Abstract**

Scagliotti GV et al. **Phase III study comparing cisplatin plus gemcitabine with cisplatin plus pemetrexed in chemotherapy-naive patients with advanced-stage non-small-cell lung cancer.** *J Clin Oncol* 2008;26(21):3543-51. **Abstract**

Stinchcombe TE et al. **Phase I trial of nanoparticle albumin-bound paclitaxel in combination with gemcitabine in patients with thoracic malignancies.** *J Thorac Oncol* 2008;3(5):521-6. **Abstract**

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **In a clinical trial evaluating chemotherapy with concurrent or sequential cetuximab for NSCLC, the median survival was doubled for patients with an increased EGFR gene copy number by FISH (FISH-positive) compared to those with FISH-negative disease.**
   a. True
   b. False
2. **In the Phase III BeTa trial, evaluating erlotinib with or without bevacizumab as second-line therapy, which endpoint was significantly improved with the addition of bevacizumab?**
   a. Overall response rate
   b. Progression-free survival
   c. Overall survival
   d. Both a and b
   e. None of the above
3. **In a pilot trial of docetaxel/placebo compared to docetaxel/vandetanib at 100 milligrams and 300 milligrams for patients with previously treated, advanced NSCLC, patients on which regimen experienced a significantly improved time to disease progression?**
   a. Docetaxel/placebo
   b. Docetaxel/vandetanib at 100 milligrams
   c. Docetaxel/vandetanib at 300 milligrams
4. **In IPASS, patients with EGFR _____ NSCLC appeared to benefit from first-line therapy with gefitinib compared to carboplatin/paclitaxel.**
   a. Mutation-positive
   b. Mutation-negative
   c. Neither of the above
5. **In the FLEX trial, the addition of cetuximab to cisplatin/vinorelbine as first-line therapy for NSCLC demonstrated a modest improvement in _____.**
   a. Overall survival
   b. Progression-free survival
   c. Both a and b
   d. None of the above
6. **Which of the following is useful in selecting patients who may benefit from erlotinib in the treatment of NSCLC?**
   a. Presence of EGFR mutation
   b. EGFR FISH amplification
   c. Both of the above
   d. None of the above
7. **In a Phase II trial evaluating erlotinib with or without carboplatin/paclitaxel for patients with advanced NSCLC, the preliminary six-month progression-free survival rate was not significantly higher for patients with EGFR-activating mutations.**
   a. True
   b. False
8. **In a randomized Phase III trial, patients with chemotherapy-naïve NSCLC who received pemetrexed/cisplatin had a better overall survival rate than those treated with gemcitabine/cisplatin if their disease was of which histologic subtype?**
   a. Adenocarcinoma
   b. Squamous cell disease
   c. Both a and b
   d. None of the above
9. **For patients with resectable NSCLC, the BEACON trial is evaluating preoperative chemotherapy with _____.**
   a. Gefitinib
   b. Erlotinib
   c. Bevacizumab
   d. Both b and c
   e. None of the above
10. **For patients with resectable NSCLC, the ECON trial is evaluating preoperative chemotherapy with _____.**
    a. Gefitinib
    b. Erlotinib
    c. Bevacizumab
    d. Both b and c
    e. None of the above

Post-test answer key: 1a, 2d, 3b, 4a, 5a, 6c, 7b, 8a, 9c, 10b

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Lung Cancer Update — Issue 1, 2009

Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART ONE — Please tell us about your experience with this educational activity

BEFORE completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

- **IPASS results: First-line gefitinib versus chemotherapy for patients highly selected for response to EGFR TKIs** 4 3 2 1
- **BeTa: Improvement in progression-free survival with the addition of bevacizumab to erlotinib as second-line therapy for advanced NSCLC** 4 3 2 1
- **Perspective on the FLEX trial: Cetuximab in combination with cisplatin/vinorelbine** 4 3 2 1
- **Vascular disrupting agents in NSCLC** 4 3 2 1
- **Role of histology and molecular biomarkers in treatment decision-making in NSCLC** 4 3 2 1

AFTER completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

- **IPASS results: First-line gefitinib versus chemotherapy for patients highly selected for response to EGFR TKIs** 4 3 2 1
- **BeTa: Improvement in progression-free survival with the addition of bevacizumab to erlotinib as second-line therapy for advanced NSCLC** 4 3 2 1
- **Perspective on the FLEX trial: Cetuximab in combination with cisplatin/vinorelbine** 4 3 2 1
- **Vascular disrupting agents in NSCLC** 4 3 2 1
- **Role of histology and molecular biomarkers in treatment decision-making in NSCLC** 4 3 2 1

Was the activity evidence based, fair, balanced and free from commercial bias?

☐ Yes ☐ No

If no, please explain: .....

Will this activity help you improve patient care?

☐ Yes ☐ No ☐ Not applicable

If no, please explain: .....

Did the activity meet your educational needs and expectations?

☐ Yes ☐ No

If no, please explain: .....

Please respond to the following LEARNER statements by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = Learning objective not met N/A = Not applicable

As a result of this activity, I will be able to:

- Utilize clinical characteristics and tumor biomarkers in treatment decision-making for patients with lung cancer. ..... 4 3 2 1 N/M N/A
- Formulate an evidence-based algorithm for the use of adjuvant chemotherapy in localized non-small cell lung cancer (NSCLC). ..... 4 3 2 1 N/M N/A
- Communicate the benefits and risks of induction chemotherapy and concurrent chemoradiation therapy when recommending treatment strategies to patients with Stage III NSCLC. ..... 4 3 2 1 N/M N/A
- Integrate emerging data on the combined use of cytotoxic and biologic agents when selecting therapy for the first-line and subsequent care of patients with advanced NSCLC. ..... 4 3 2 1 N/M N/A
- Identify patients with NSCLC who are most likely to benefit from treatment with EGFR tyrosine kinase inhibitors and monoclonal antibodies. ..... 4 3 2 1 N/M N/A
- Assess the scientific and therapeutic applications of neoadjuvant systemic therapy for patients with locally advanced NSCLC. ..... 4 3 2 1 N/M N/A
- Apply the results of recently reported Phase III trials to the care of patients with extensive-stage small cell lung cancer. ..... 4 3 2 1 N/M N/A
- Counsel appropriately selected patients with lung cancer about the availability of ongoing clinical trials in which they may be eligible to participate. ..... 4 3 2 1 N/M N/A

What other practice changes will you make or consider making as a result of this activity?

.....

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

What additional information or training do you need on the activity topics or other oncology-related topics?

.....

Additional comments about this activity:

.....

.....

As part of our ongoing, continuous quality-improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate your willingness to participate in such a survey.

☐ Yes, I am willing to participate in a follow-up survey. ☐ No, I am not willing to participate in a follow-up survey.

PART TWO — Please tell us about the editor and faculty for this educational activity

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
Roy S Herbst, MD, PhD	4 3 2 1	4 3 2 1
Primo N Lara Jr, MD	4 3 2 1	4 3 2 1
Giuseppe Giaccone, MD, PhD	4 3 2 1	4 3 2 1
Naiyer A Rizvi, MD	4 3 2 1	4 3 2 1
Editor	**Knowledge of subject matter**	**Effectiveness as an educator**
Neil Love, MD	4 3 2 1	4 3 2 1

Please recommend additional faculty for future activities:

.....

Other comments about the editor and faculty for this activity:

.....

REQUEST FOR CREDIT — Please print clearly

Name: ..... Specialty: .....

Professional Designation:

☐ MD ☐ DO ☐ PharmD ☐ NP ☐ RN ☐ PA ☐ Other .....

Medical License/ME Number: ..... Last 4 Digits of SSN (required): .....

Street Address: ..... Box/Suite: .....

City, State, Zip: .....

Telephone: ..... Fax: .....

Email: .....

Research To Practice designates this educational activity for a maximum of 3 *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

I certify my actual time spent to complete this educational activity to be _____ hour(s).

Signature: ..... Date: .....

To obtain a certificate of completion and receive credit for this activity, please complete the Post-test, fill out the Educational Assessment and Credit Form and fax both to (800) 447-4310, or mail both to Research To Practice, One Biscayne Tower, 2 South Biscayne Boulevard, Suite 3600, Miami, FL 33131. You may also complete the Post-test and Educational Assessment online at www.ResearchToPractice.com/LCU/CME.

LCU109

Lung Cancer™ UPDATE

Contact Information	Neil Love, MD Research To Practice One Biscayne Tower 2 South Biscayne Boulevard, Suite 3600 Miami, FL 33131 Fax: (305) 377-9998 Email: DrNeilLove@ResearchToPractice.com
For CME/CNE Information	Email: CE@ResearchToPractice.com

Lung Cancer™ UPDATE

This program is supported by educational grants from
Bristol-Myers Squibb Company, Genentech BioOncology/OSI
Oncology, ImClone Systems Incorporated and Sanofi-Aventis.

Research
To Practice®

Sponsored by Research To Practice.

Last review date: February 2009
Release date: February 2009
Expiration date: February 2010
Estimated time to complete: 3 hours