LCU | 2008 VOL 5 | ISSUE 1

Lung Cancer™ UPDATE

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

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INTERVIEWS

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CME Certified

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Lung Cancer Update
A Continuing Medical Education Audio Series

STATEMENT OF NEED/TARGET AUDIENCE

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 modest, and about 85 percent of patients who develop lung cancer will die from it. In addition, a sense of therapeutic nihilism has pervaded the medical community in the past. Chemotherapy, surgery and radiation therapy have had modest effects on patient outcomes. However, recent improvements have been seen in time to progression and survival in lung cancer clinical trials. Published results from ongoing clinical trials lead to the continuous emergence of new therapeutic agents and changes in the indications for existing treatments. In order to offer optimal patient care — including the option of clinical trial participation — practicing medical oncologists, radiation oncologists, hematologists and hematology/oncology fellows must be well informed of these advances. To bridge the gap between research and patient care, *Lung Cancer Update* features one-on-one discussions with leading oncology investigators. By providing access to the latest research developments and expert perspectives, this CME program assists physicians with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Describe the key clinical and pathologic risk factors that influence clinician selection of the medical and surgical management of lung cancer.
- Develop an evidence-based algorithm for the initial treatment of localized non-small cell lung cancer (NSCLC), exploring the roles of neoadjuvant and adjuvant systemic therapy.
- Discuss the existing data and emerging research focusing on the optimal management of locally advanced Stage III NSCLC, incorporating the concepts of induction chemotherapy, concomitant chemoradiation therapy and the role of consolidation regimens.
- Review the existing research that supports alternative doses, formulations and schedules of the commonly used adjuvant and metastatic chemotherapeutic regimens.
- Describe the emerging role of novel taxane delivery systems and associated efficacy and tolerability findings.
- Review and critique the emerging clinical research data and ongoing trials evaluating the future roles of novel molecular targeted agents in lung cancer.
- Describe the contributory roles of surgery, radiation therapy (local and prophylactic cranial irradiation) and chemotherapy in the management of limited- and/or extensive-stage SCLC.
- Counsel appropriately selected patients about the availability of ongoing clinical trial participation.

PURPOSE OF THIS ISSUE OF *LUNG CANCER UPDATE*

The purpose of Issue 1 of *Lung Cancer Update* is to support the learning objectives by featuring the perspectives of Drs Bunn, Hanna and Wozniak on the integration of emerging clinical research data into the management of lung cancer.

ACCREDITATION STATEMENT

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This program is supported by educational grants from Abraxis BioScience, AstraZeneca Pharmaceuticals LP, Genentech BioOncology/OSI Pharmaceuticals Inc and Sanofi-Aventis.

TABLE OF CONTENTS

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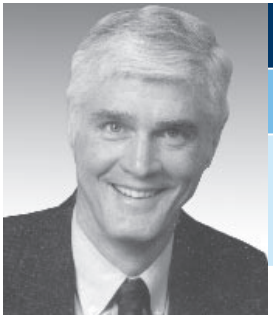


INTERVIEW

Paul A Bunn Jr, MD

Dr Bunn is Professor and Director at the University of Colorado Cancer Center and is James Dudley Chair in Cancer Research in Denver, Colorado.

Tracks 1-18

Select Excerpts from the Interview

Track 2

DR LOVE: Can you review what we know about the use of bevacizumab to treat metastatic NSCLC?

DR BUNN: Two randomized Phase III trials have evaluated bevacizumab (Sandler 2006; Manegold 2007). One from the US, ECOG-E4599, evaluated it in combination with carboplatin/paclitaxel. The addition of bevacizumab demonstrated a survival benefit with a hazard ratio that was clinically relevant

(Sandler 2006; [1.1]). So for patients like the ones who were included in ECOG-E4599 (ie, nonsquamous tumors, no brain metastases, no hemoptysis, no anticoagulants), I believe most oncologists in the US would use bevacizumab. I would.

It is reasonable to use bevacizumab for patients who are similar to those who were eligible for ECOG-E4599. However, some questions remain. Bevacizumab has been used for patients with gliomas, and an ongoing study is testing it in patients with brain metastases.

Currently, if you have a patient with a radiated brain metastasis, you should not administer bevacizumab. If a patient is receiving warfarin or subcutaneous heparin, the administration of bevacizumab is also questionable.

Two major differences arose between the AVAiL trial and the ECOG-E4599 trial. The first difference was that the chemotherapy in the AVAiL study was gemcitabine based instead of paclitaxel based. The second difference was that the AVAiL trial used two every three-week doses of bevacizumab, 7.5 mg/kg and 15 mg/kg.

1.1

ECOG-E4599: Efficacy of the Addition of Bevacizumab (B) to Paclitaxel (P) and Carboplatin (C) in Previously Untreated Metastatic Nonsquamous NSCLC

Endpoint	PC (n = 433)	PCB (n = 417)	HR (95% CI)	*p*-value
Median OS	10.3 months	12.3 months	0.79 (0.67-0.92)	0.003
Two-year OS	15%	23%	—	—
Median PFS	4.5 months	6.2 months	0.66 (0.57-0.77)	<0.001
Overall response	15%	35%	—	<0.001

OS = overall survival
PFS = progression-free survival

SOURCE: Sandler A et al. *N Engl J Med* 2006;355(24):2542-50. **Abstract**

1.2

The AVAiL Study: Progression-Free Survival (PFS) After Cisplatin/Gemcitabine with or without Bevacizumab for Chemotherapy-Naïve Patients with Nonsquamous Advanced or Recurrent NSCLC

	Median PFS	Hazard ratio	*p*-value
Cisplatin/gemcitabine + placebo	6.1 months	Reference	Reference
Cisplatin/gemcitabine + bevacizumab 7.5 mg/kg	6.7 months	0.75	0.0026
Cisplatin/gemcitabine + bevacizumab 15 mg/kg	6.5 months	0.82	0.0301

SOURCE: Manegold C et al. *Proc ASCO* 2007;**Abstract LBA7514**.

The primary endpoint of the AVAiL study was progression-free survival, and that endpoint was met. That has been presented, but the survival data have not been presented (Manegold 2007; [1.2]).

For progression-free survival, no difference was observed between the 7.5-mg/kg dose and the 15-mg/kg dose every three weeks, and the improvements seemed less striking than those in ECOG-E4599.

We do not know whether the choice of chemotherapy matters or whether the dose of bevacizumab matters. My inclination is to continue using paclitaxel/carboplatin with bevacizumab at a dose of 15 mg/kg every three weeks.

Tracks 5-6

DR LOVE: What do we know about combining other agents with bevacizumab?

DR BUNN: We have some data in the second-line setting. A randomized Phase II trial compared docetaxel or pemetrexed alone, docetaxel or pemetrexed with bevacizumab or erlotinib with bevacizumab.

The patients in the arms that received bevacizumab seemed to do better than the patients who received chemotherapy alone (Fehrenbacher 2006; [1.3]). The data from this study suggest that two more drugs — pemetrexed and docetaxel — are useful with bevacizumab.

DR LOVE: How do you think through treatment decisions in the second line?

DR BUNN: Second-line treatment is an issue because several drugs — docetaxel, pemetrexed, gefitinib and erlotinib — have been tested and have a

1.3

Phase II Trial of Bevacizumab with Chemotherapy or Erlotinib Compared to Chemotherapy Alone in Recurrent or Refractory Non-Small Cell Lung Cancer: Efficacy Data

	Chemotherapy* alone (n = 41)	Chemotherapy* + bevacizumab (n = 40)	Bevacizumab + erlotinib (n = 39)
Progression-free survival			
Median	3.0 months	4.8 months	4.4 months
Six-month rate	21.5%	30.5%	33.6%
Hazard ratio (95% CI)	NA	0.66 (0.38-1.16)	0.72 (0.42-1.23)
Overall survival			
Six-month rate	62.4%	72.1%	78.3%
Response rate			
CR/PR	12.2%	12.5%	17.9%
CR/PR/SD	39.0%	52.5%	51.3%

* Docetaxel or pemetrexed

SOURCE: Fehrenbacher L et al. *Proc ASCO* 2006;**Abstract 7062**.

1.4

The INTEREST Trial: A Randomized Phase III Trial of Gefitinib versus Docetaxel for Patients with Platinum-Treated NSCLC

Accrual: 1,466 (Closed)

Eligibility

- ≥18 years of age with progressive or recurrent disease after chemotherapy
- Life expectancy ≥ 8 wk
- Failed at least one platinum-based chemotherapy regimen
- PS 0-2

R → Gefitinib 250 mg/d

R → Docetaxel 75 mg/m^2 q3wk

Overall survival (OS) in the per-protocol population (n = 1,433)

	Gefitinib (n = 723)	Docetaxel (n = 710)	HR (96% CI)
Events	593 (82%)	576 (81.1%)	1.02 (0.91-1.15)
Median OS	7.6 mo	8.0 mo	
One-year survival	32%	34%	
Treatment-related adverse event (AE) summary			
Grade III/IV AEs	8.5%	40.7%	
Serious AEs	3.8%	18.2%	
Deaths caused by AEs	0.8%	2.1%	
Study discontinuations caused by AEs	4.1%	10.9%	

SOURCE: Douillard J-Y et al. *Proc 12th World Conference on Lung Cancer* 2007;**Abstract PRS-02**.

beneficial effect. The largest comparative study, which was presented in Seoul in 2007, was the INTEREST trial.

Docetaxel was compared to gefitinib, and there was absolutely no difference. Those results might lead people to use gefitinib because less toxicity occurred with gefitinib (Douillard 2007; [1.4]).

In the trial comparing pemetrexed to docetaxel, survival was again identical, but pemetrexed was the winner because it was associated with much less toxicity (Hanna 2004). A comparison of pemetrexed versus gefitinib or erlotinib has not been completed.

Track 7

DR LOVE: You mentioned that you tend to use carboplatin/paclitaxel. What are your thoughts about *nab* paclitaxel in lung cancer?

DR BUNN: The Phase II trials are complete (Reynolds 2007; Hawkins 2007; Greco 2006), and *nab* paclitaxel is active. It is similar to paclitaxel but is more

convenient. Ongoing randomized Phase III trials are largely being conducted outside of the US.

If the findings are negative, that will probably be the end of the drug in lung cancer. If they're positive, the question is, how would *nab* paclitaxel be used? And that depends on the magnitude of the differences shown in the Phase III trials. In the US, I believe *nab* paclitaxel will be used by some clinicians.

Track 13

DR LOVE: Where are we in terms of adjuvant trials for NSCLC?

DR BUNN: Currently, the hope is that three important adjuvant trials — ECOG-E1505, EORTC-08021 and RADIANT — will all accrue. The RADIANT trial, which is testing erlotinib (1.5), started first. In that study, patients may or may not have received adjuvant chemotherapy.

A patient with Stage IB disease who is not treated in the adjuvant setting is eligible for the study. A patient with Stage II disease who has experienced side effects from surgery and does not want chemotherapy is also eligible, as is the patient who has completed adjuvant chemotherapy. To participate in the study, the patient's tumor must be IHC-positive and/or FISH-positive for EGFR.

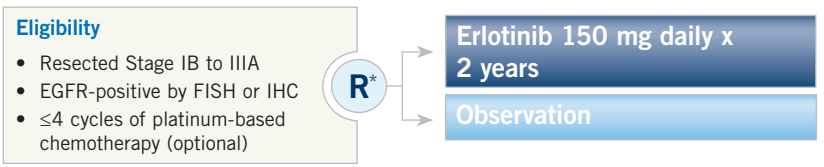
DR LOVE: What about the off-protocol use of erlotinib for such patients as an alternative strategy?

DR BUNN: Because we have no data, it is not done much. I have treated one or two patients that way. It is not something that I recommended, but because the patients were interested and wanted to do it, I did not prevent them from doing it. If it were me and my tumor was FISH-positive for EGFR, I would do it. ■

1.5

The RADIANT Trial: A Phase III Study of Erlotinib or Placebo with or without Adjuvant Chemotherapy for Patients with Resected, EGFR-Positive NSCLC

Protocol IDs: OSI-774-302, NCT00373425
Target accrual: 945 (Open)



* Stratified by histology (squamous versus other), gender, age, EGFR status, smoking status and adjuvant chemotherapy

SOURCES: NCI Physician Data Query, December 2007; Wakelee H et al. *Oncologist* 2007;12:331-7. **Abstract**

SELECT PUBLICATIONS

Belani CP et al. **Multicenter, randomized trial for stage IIIB or IV non-small-cell lung cancer using weekly paclitaxel and carboplatin followed by maintenance weekly paclitaxel or observation.** *J Clin Oncol* 2003;21(15):2933-9. **Abstract**

Cho BC et al. **Phase II study of erlotinib in advanced non-small-cell lung cancer after failure of gefitinib.** *J Clin Oncol* 2007;25(18):2528-33. **Abstract**

Douillard J-Y et al. **Gefitinib (IRESSA) versus docetaxel in patients with locally advanced or metastatic non-small-cell lung cancer pre-treated with platinum-based chemotherapy: A randomized, open-label Phase III study (INTEREST).** *Proc 12th World Conference on Lung Cancer* 2007;**Abstract PRS-02**.

Fehrenbacher L et al. **A phase II, multicenter, randomized clinical trial to evaluate the efficacy and safety of bevacizumab in combination with either chemotherapy (docetaxel or pemetrexed) or erlotinib hydrochloride compared with chemotherapy alone for treatment of recurrent or refractory non-small cell lung cancer.** *Proc ASCO* 2006;**Abstract 7062**.

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**

Gradishar WJ et al. **Phase III trial of nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer.** *J Clin Oncol* 2005;23(31):7794-803. **Abstract**

Greco A et al. **Albumin bound paclitaxel wkly + carboplatin: First-line therapy for advanced NSCLC.** *Proc Chemotherapy Foundation Symposium XXIV* 2006. No abstract available

Grønberg BH et al. **A phase III study by the Norwegian Lung Cancer Group: Pemetrexed + carboplatin vs gemcitabine + carboplatin as first-line chemotherapy in stage IIIB/IV non-small cell lung cancer.** IASLC Meeting 2007;**Abstract A3-04**.

Hanna N et al. **Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy.** *J Clin Oncol* 2004;22(9):1589-97. **Abstract**

Hawkins MJ et al. **Study of three weekly *nab*-paclitaxel regimens in combination with carboplatin as first-line therapy in advanced non-small cell lung cancer (NSCLC).** *Proc ASCO* 2007;**Abstract 7659**.

Heymach JV et al. **A phase II trial of ZD6474 plus docetaxel in patients with previously treated NSCLC: Follow-up results.** *Proc ASCO* 2006;**Abstract 7016**.

Le Calvez F et al. **TP53 and KRAS mutation load and types in lung cancers in relation to tobacco smoke: Distinct patterns in never, former, and current smokers.** *Cancer Res* 2005;65(12):5076-83. **Abstract**

Manegold C et al. **Randomized, double-blind multicentre phase III study of bevacizumab in combination with cisplatin and gemcitabine in chemotherapy-naïve patients with advanced or recurrent non-squamous non-small cell lung cancer (NSCLC): BO17704.** *Proc ASCO* 2007;**Abstract LBA7514**.

Reynolds C et al. **An open-label, phase II trial of nanoparticle albumin bound paclitaxel (*nab*-paclitaxel), carboplatin, and bevacizumab in first-line patients with advanced non-squamous non-small cell lung cancer (NSCLC).** *Proc ASCO* 2007;**Abstract 7610**.

Sandler A et al. **Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer.** *N Engl J Med* 2006;355(24):2542-50. **Abstract**

Scagliotti GV et al. **A randomized phase III trial of cisplatin and pemetrexed versus cisplatin and gemcitabine in patients with locally advanced or metastatic non-small cell lung cancer.** *Proc 12th World Conference on Lung Cancer* 2007;**Abstract PRS-03**.

Toyooka S et al. **The impact of sex and smoking status on the mutational spectrum of epidermal growth factor receptor gene in non small cell lung cancer.** *Clin Cancer Res* 2007;13(19):5763-8. **Abstract**

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

INTERVIEW

Nasser H Hanna, MD

Dr Hanna is Associate Professor in the Department of Medicine's Division of Hematology/Oncology at Indiana University Medical Center's School of Medicine in Indianapolis, Indiana.

Tracks 1-18

Select Excerpts from the Interview

Tracks 1, 3

DR LOVE: What are your thoughts about the ECOG-E1505 adjuvant study evaluating bevacizumab?

DR HANNA: ECOG-E1505 is a randomized Phase III study that will treat patients with resected, Stage IB to IIIA NSCLC. Patients will receive one of three cisplatin-based chemotherapy regimens — cisplatin/gemcitabine, cisplatin/docetaxel or cisplatin/vinorelbine — with or without bevacizumab (2.1).

DR LOVE: Currently, in your own practice outside of a protocol setting, how are you approaching the selection of chemotherapy?

DR HANNA: I use cisplatin-based therapy unless there is a contraindication such as modest renal insufficiency, in which case I administer carboplatin. I believe little difference exists between the two agents, which may be supported by early data from a European neoadjuvant trial presented at ASCO this year (Milleron 2007).

DR LOVE: Which agent do you generally combine with cisplatin in the adjuvant setting?

DR HANNA: I generally use docetaxel. The majority of data we have from the adjuvant setting are with cisplatin/vinorelbine. However, you want to use your best regimens from the metastatic setting in the adjuvant setting. Trials have been conducted comparing cisplatin/docetaxel to cisplatin/vinorelbine (Fossella 2003; Douillard 2005; [3.1]) or single-agent docetaxel to single-agent vinorelbine, in which docetaxel was a more active and effective agent (Fossella 2000; Kudoh 2006). That is why I use cisplatin/docetaxel.

2.1

Phase III Study of Adjuvant Chemotherapy with or without Bevacizumab for Patients with Completely Resected Stage IB-IIIA NSCLC

Protocol ID: ECOG-E1505; Target Accrual: 1,500

* Patients are stratified according to type of chemotherapy, stage, histology and gender.

Eligibility

- Resection within the past six to 12 weeks
- ECOG performance status 0-1
- No history of CVA or TIA
- History of myocardial infarction or angina acceptable if no evidence of active disease within the past 12 months

SOURCE: NCI Physician Data Query, January 2008.

Track 9

DR LOVE: Can you discuss the Hoosier Oncology Group (HOG) trial data you presented at ASCO 2007?

DR HANNA: In 2003, SWOG published results from their Phase II trial, S9504, which included 83 patients with Stage IIIB disease who were treated with two cycles of cisplatin/etoposide concurrent with 61 Gray of radiation followed by three cycles of docetaxel. The median survival was 26 months (Gandara 2003, 2006). This population should have had a median survival of about 13 months. They had a five-year survival of 29 percent. Historically, that group should have had a five-year survival of five, seven or eight percent.

This regimen engendered a lot of enthusiasm and became a de facto standard for many physicians based on a single, small Phase II trial. We sought to confirm that the strategy was effective and conducted a randomized Phase III study for patients with Stage IIIA and Stage IIIB disease (Hanna 2007).

A total of 243 patients entered our trial. All patients received cisplatin/etoposide and concurrent radiation at 59.4 Gray. Then, after a rest period of four to eight weeks — and as long as they had not progressed and remained eligible — patients were randomly assigned to either three cycles of docetaxel or observation. We reported several provocative findings. No difference was observed in progression-free survival between the two randomization arms, and no difference was observed in overall survival. The *p*-value was 0.9 and the curves were completely superimposable (Hanna 2007). We determined that no evidence existed that consolidation docetaxel after chemoradiation therapy improves outcomes but does significantly increase risks for patients, including treatment-related death and serious toxicities such as febrile neutropenia, infections and Grade III/IV pneumonitis.

Track 15

DR LOVE: Can you discuss how vandetanib works and what we know about it in lung cancer?

DR HANNA: Vandetanib is an interesting oral agent. It is a dual EGFR and VEGFR kinase inhibitor. The questions are, is it as good of an EGFR inhibitor as erlotinib, and is it as good of a VEGF inhibitor as bevacizumab? Simply because it hits the same general pathways and targets does not mean that it will be better than administering two drugs.

At ASCO 2006, Dr Natale reported the results from a trial comparing vandetanib to gefitinib in the second-line setting. The primary endpoint of the trial was progression-free survival. Vandetanib had a higher response rate and an improved progression-free survival compared to gefitinib (Natale 2006; [2.2]). Also at ASCO 2006, Dr Heymach reported the results of a three-arm, randomized Phase II study in the second-line setting. The patients in the two arms containing vandetanib had what appeared to be an enhanced progression-free survival compared to docetaxel alone (Heymach 2006, 2007b; [2.2]).

A randomized Phase II trial, reported at ASCO 2007, evaluated carboplatin/paclitaxel with or without vandetanib as first-line therapy. The patients receiving vandetanib appeared to have an improved progression-free survival compared to those receiving chemotherapy alone (Heymach 2007a).

2.2 **Vandetanib in the Treatment of Patients with Advanced Non-Small Cell Lung Cancer Previously Treated with Platinum-Based Chemotherapy**

	Vandetanib[1] (n = 83)	Gefitinib[1] (n = 85)	Docetaxel + placebo[2] (n = 41)	Docetaxel + vandetanib 100 mg[2] (n = 42)	Docetaxel + vandetanib 300 mg[2] (n = 44)
Median PFS	11.0 wks	8.1 wks	12.0 wks	18.7 wks	17.0 wks
Hazard ratio (95% CI)	0.69 (0.50-0.96)	—	NA	0.64 (0.38-1.05)	0.83 (0.50-1.36)
p-value	0.025	—	NA	0.074	0.231

SOURCES: [1] Natale RB et al. *Proc ASCO* 2006;**Abstract 7000**; [2] Heymach JV et al. *J Clin Oncol* 2007b;25(27):4270-7. **Abstract**

Track 18

DR LOVE: How do you approach first-line therapy for patients with metastatic NSCLC?

DR HANNA: If a patient has a performance status (PS) of 3 or 4, the right treatment is best supportive care. If the patient has a PS of 2 and in addition is experiencing significant loss of appetite, loss of weight and comorbidities, then I believe the appropriate practice is best supportive care unless he or she is a never smoker. Then I would consider single-agent erlotinib.

For patients with a PS of 0 or 1 and no contraindications to chemotherapy, I believe a platinum-based, two-drug regimen is standard. For patients who don't have brain metastases, squamous histology, a history of hemoptysis or uncontrolled hypertension, the addition of bevacizumab is reasonable.

I treat those patients initially with two courses of chemotherapy and repeat their CT scan. If they appear to obtain clinical benefit, I administer four courses of chemotherapy. Because the Sandler study continued patients on bevacizumab (Sandler 2006), I administer it as maintenance until time of progression.

DR LOVE: Which chemotherapy regimens do you think are reasonable to use in the first-line setting with bevacizumab?

DR HANNA: The only randomized Phase III data are with carboplatin/paclitaxel (Sandler 2006; [1.1]) and cisplatin/gemcitabine (Manegold 2007; [1.2]). I believe it's reasonable to use either of those regimens with bevacizumab. Bevacizumab is likely to be safe and effective with other regimens, too.

We will be seeing data with docetaxel/platinum and pemetrexed/platinum. At ASCO 2007, Dr Patel reported an improved response rate and acceptable toxicities with carboplatin/pemetrexed and bevacizumab (Patel 2007). I believe those types of regimens would be perfectly acceptable. ■

SELECT PUBLICATIONS

Douillard JY et al. **Sequential two-line strategy for stage IV non-small-cell lung cancer: Docetaxel-cisplatin versus vinorelbine-cisplatin followed by cross-over to single-agent docetaxel or vinorelbine at progression: Final results of a randomised phase II study.** *Ann Oncol* 2005;16(1):81-9. **Abstract**

Fossella F et al. **Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: The TAX 326 study group.** *J Clin Oncol* 2003;21(16):3016-24. **Abstract**

Fossella FV et al. **Randomized phase III trial of docetaxel versus vinorelbine or ifosfamide in patients with advanced non-small-cell lung cancer previously treated with platinum-containing chemotherapy regimens. The TAX 320 Non-Small Cell Lung Cancer Study Group.** *J Clin Oncol* 2000;18(12):2354-62. **Abstract**

Gandara DR et al. **Long-term survival with concurrent chemoradiation therapy followed by consolidation docetaxel in stage IIIB non-small-cell lung cancer: A phase II Southwest Oncology Group study (S9504).** *Clin Lung Cancer* 2006;8(2):116-21. **Abstract**

Gandara DR et al. **Consolidation docetaxel after concurrent chemoradiotherapy in stage IIIB non-small-cell lung cancer: Phase II Southwest Oncology Group Study S9504.** *J Clin Oncol* 2003;21(10):2004-10. **Abstract**

Hanna NH et al. **Phase III trial of cisplatin (P) plus etoposide (E) plus concurrent chest radiation (XRT) with or without consolidation docetaxel (D) in patients (pts) with inoperable stage III non-small cell lung cancer (NSCLC): HOG LUN 01-24/USO-023.** *Proc ASCO* 2007;**Abstract 7512**.

Heymach JV et al. **Randomized phase II study of vandetanib (VAN) alone or in combination with carboplatin and paclitaxel (CP) as first-line treatment for advanced non-small cell lung cancer (NSCLC).** *Proc ASCO* 2007a;**Abstract 7544**.

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* 2007b;25(27):4270-7. **Abstract**

Heymach JV et al. **A phase II trial of ZD6474 plus docetaxel in patients with previously treated NSCLC: Follow-up results.** *Proc ASCO* 2006;**Abstract 7016**.

Kudoh S et al. **Phase III study of docetaxel compared with vinorelbine in elderly patients with advanced non-small-cell lung cancer: Results of the West Japan Thoracic Oncology Group trial (WJTOG 9904).** *J Clin Oncol* 2006;24(22):3657-63. **Abstract**

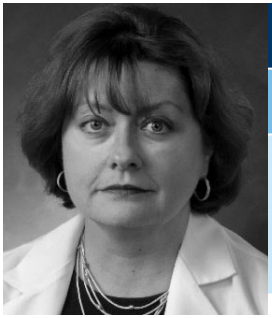
Manegold C et al. **Randomized, double-blind multicentre phase III study of bevacizumab in combination with cisplatin and gemcitabine in chemotherapy-naïve patients with advanced or recurrent non-squamous non-small cell lung cancer (NSCLC): BO17704.** *Proc ASCO* 2007;**Abstract LBA7514**.

Milleron B et al. **IFCT0002 phase III study comparing a preoperative (PRE) and a perioperative (PERI) chemotherapy with two different CT regimens in resectable non-small cell lung cancer (NSCLC): Early results.** *Proc ASCO* 2007;**Abstract 7519**.

Natale RB et al. **ZD6474 versus gefitinib in patients with advanced NSCLC: Final results from a two-part, double-blind, randomized phase II trial.** *Proc ASCO* 2006;**Abstract 7000**.

Patel JD et al. **Pemetrexed and carboplatin plus bevacizumab for advanced non-squamous non-small cell lung cancer (NSCLC): Preliminary results.** *Proc ASCO* 2007;**Abstract 7601**.

Sandler A et al. **Paclitaxel-carboplatin alone or with bevacizumab for non-small-cell lung cancer.** *N Engl J Med* 2006;355(24):2542-50. **Abstract**



INTERVIEW

Antoinette J Wozniak, MD

Dr Wozniak is Professor of Medicine and Oncology and Leader of the Thoracic Multidisciplinary Team at Wayne State University's Karmanos Cancer Institute in Detroit, Michigan.

Tracks 1-17

Select Excerpts from the Interview

Tracks 1-2

DR LOVE: How do you approach the selection of chemotherapy in the adjuvant setting?

DR WOZNIAK: Whether to use cisplatin or carboplatin is a big question. In

practice, I believe most physicians prefer using carboplatin because it's easier. All the evidence, even in the advanced-disease setting, indicates that cisplatin is likely more effective. It may not make a difference for patients with metastatic disease, but it may make a difference in the adjuvant setting. Generally, I use cisplatin whenever possible, combined with either vinorelbine or docetaxel. Most of the trials, including the Canadian trial (Winton 2005) and the ANITA trial (Douillard 2005, 2006), used vinorelbine. In IALT, approximately 25 percent of the patients received vinorelbine and approximately half of the patients received etoposide (Arriagada 2004).

In advanced disease, TAX-326 compared cisplatin/vinorelbine to cisplatin/docetaxel and carboplatin/docetaxel. The cisplatin/docetaxel arm was better in that trial (Fossella 2003; [3.1]), which is why many people use it as adjuvant treatment.

3.1

Phase III Randomized Trial (TAX-326) of Docetaxel with Platinum Combination versus Vinorelbine/Cisplatin for Patients with Previously Untreated Advanced NSCLC: Comparison of Docetaxel/Cisplatin and Vinorelbine/Cisplatin*

	Docetaxel/cisplatin (n = 408)	Vinorelbine/cisplatin (n = 404)	*p*-value
Overall median survival (95% CI)	11.3 months (10.1-12.4)	10.1 months (9.2-11.3)	0.044†‡
Estimated one-year survival (95% CI)	46% (42%-51%)	41% (36%-46%)	—
Estimated two-year survival (95% CI)	21% (16%-25%)	14% (10%-18%)	—
Overall response rate (95% CI)	31.6% (27.1%-36.4%)	24.5% (20.4%-29.0%)	0.029§

CI = confidence interval
* Comparison of docetaxel/carboplatin and vinorelbine/cisplatin not presented in this table;
† Nonparametric, covariate-adjusted log-rank test; ‡ hazard ratio = 1.183;
§ Fisher exact test

SOURCE: Fossella F et al. *J Clin Oncol* 2003;21(16):3016-24. **Abstract**

Tracks 6, 8

DR LOVE: Can you discuss the SWOG-S0533 study for patients with unresectable Stage III NSCLC?

DR WOZNIAK: It is still in the early stages of accrual. The goal of the trial is to offer bevacizumab to these patients. Not a lot is known about the combination of chemotherapy, radiation and bevacizumab. So the trial has two groups of patients and three cohorts of treatment (3.2).

One of the groups of patients will be considered at low risk with regard to hemoptysis associated with bevacizumab, and the other group will be consid-

3.2

Phase I/II Pilot Study of Induction Therapy with Cisplatin/Etoposide/Radiation Therapy with or without Bevacizumab Followed by Consolidation with Docetaxel/Bevacizumab for Patients with Newly Diagnosed, Unresectable Stage III NSCLC

Protocol ID: SWOG-S0533
Target Accrual: 182 (Open) Trial Start Date: June 15, 2006

Induction therapy

- Cisplatin/etoposide + thoracic radiation therapy
- Cisplatin/etoposide + thoracic radiation therapy + **bevacizumab** (d15, 36, 57)
- Cisplatin/etoposide + thoracic radiation therapy + **bevacizumab** (d1, 22, 43)

Three to six weeks after induction therapy, all patients receive consolidation therapy.

Consolidation therapy

- **Docetaxel** + **bevacizumab** (with **filgrastim** or **pegfilgrastim**) q3wk x 3

Primary Endpoints
Frequency and severity of toxicity

Secondary Endpoints
Progression-free survival, overall survival and response

Stratification
High versus low risk

Eligibility

- Stage IIIA (N2) disease meeting the following criteria:
  N2 mediastinal lymph nodes must be multiple or bulky on CT scan or x-ray so that the patient is not a candidate for induction chemotherapy or chemoradiation therapy followed by surgical resection
- Stage IIIB disease with histologically or radiographically confirmed positive N3 nodes
- T4 lesions of any size that invade the mediastinum, heart, great vessels, trachea, esophagus, vertebral body or cranium

SOURCE: NCI Physician Data Query, January 2008.

ered at high risk. High risk is defined by predominantly squamous histology, a history of hemoptysis or a tumor that is fairly central, near a major blood vessel or with some cavitation. The low-risk and the high-risk groups will accrue independently.

The first cohort of patients will receive cisplatin/etoposide and radiation therapy. After a break, they will receive bevacizumab with docetaxel consolidation. If the side effects are acceptable in the high-risk and low-risk groups, then we move to the second cohort. It is similar to a Phase I study.

DR LOVE: In the second cohort, will you add bevacizumab during chemoradiation therapy?

DR WOZNIAK: Yes, in the midst of it. Then, if we reach the third cohort,

bevacizumab will be administered at the beginning of chemoradiation therapy. We have another trial evaluating cisplatin/pemetrexed with radiation therapy in Stage III disease. This trial was designed before the HOG trial results were available (Hanna 2007), and we're using docetaxel consolidation. Pemetrexed is another drug that can be administered at full doses with radiation therapy. I believe it is an up-and-coming drug in lung cancer and that it may be the drug to use in Stage III disease. We decided to keep docetaxel consolidation because a different chemotherapy agent is administered with the radiation therapy, and this may be good.

DR LOVE: What data do we have with pemetrexed in combination with chemoradiation therapy in Stage III disease?

DR WOZNIAK: Studies are ongoing. Our trial is new, but in the patients we've treated, it's been tolerable. I can't tell you anything about survival because we don't know that yet. Pemetrexed is well tolerated when administered in concurrence with radiation therapy. Patients are generally able to get through the entire treatment without dose reductions. Cisplatin/etoposide/radiation therapy is also well tolerated. The question is which is the better combination.

Track 13

DR LOVE: What is your treatment algorithm for metastatic disease in a nonsmoker or a nonsmoker with EGFR-positive disease?

DR WOZNIAK: The only factor I consider is nonsmoking status because that seems to have the strongest support for using an EGFR inhibitor. In the clinical setting, I believe the standard approach up front is still systemic chemotherapy. As first-line therapy, I use carboplatin/paclitaxel or carboplatin/gemcitabine. In terms of what to do with the never smoker — someone who's smoked fewer than 100 cigarettes in his or her lifetime — I will discuss the option of erlotinib. If any patients were going to respond, they would be in that particular group. The majority of patients who dramatically respond to these drugs generally do so within the first four weeks of treatment. So if someone would like that option, I don't believe there's anything wrong with it.

DR LOVE: Would you consider it as first-line therapy?

DR WOZNIAK: For a never smoker, I would.

Track 15

DR LOVE: Can you describe the two SWOG studies that are evaluating the combination of erlotinib and bevacizumab?

DR WOZNIAK: These trials will study patients who we perceive will benefit more from erlotinib. Patients will receive the combination of erlotinib and bevacizumab, which appeared promising in other clinical trials (Groen 2007; Herbst 2005, 2007). We will also evaluate biologic correlates — mutations,

EGFR expression and FISH analysis — that will be important in order to determine whether characteristics of the tumor predict response.

DR LOVE: Are you using erlotinib/bevacizumab off study?

DR WOZNIAK: Not currently. We are participating in a Phase III study evaluating erlotinib with bevacizumab or placebo as second-line treatment. I would like to see the results of that study first.

DR LOVE: If a patient who is a never smoker, has the EGFR mutation or has FISH-positive disease responds well to chemotherapy and bevacizumab, some physicians will discontinue chemotherapy and continue treatment with bevacizumab. At some point would you add erlotinib to the bevacizumab?

DR WOZNIAK: I like to see evidence before combining certain agents, but I suspect that for that patient, even I might be willing to combine erlotinib and bevacizumab. ■

SELECT PUBLICATIONS

Arriagada R et al; International Adjuvant Lung Cancer Trial Collaborative Group. **Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer.** *N Engl J Med* 2004;350(4):351-60. **Abstract**

Douillard JY et al. **Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIA non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): A randomised controlled trial.** *Lancet Oncol* 2006;7(9):719-27. **Abstract**

Douillard J et al. **ANITA: Phase III adjuvant vinorelbine (N) and cisplatin (P) versus observation (OBS) in completely resected (stage I-III) non-small-cell lung cancer (NSCLC) patients (pts): Final results after 70-month median follow-up. On behalf of the Adjuvant Navelbine International Trialist Association.** *Proc ASCO* 2005;**Abstract 7013**.

Fossella F et al. **Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: The TAX 326 study group.** *J Clin Oncol* 2003;21(16):3016-24. **Abstract**

Groen HJ et al. **A phase II study of erlotinib (E) and bevacizumab (B) in patients (pts) with previously untreated stage IIIB/IV non-small cell lung cancer (NSCLC).** *Proc ASCO* 2007;**Abstract 7625**.

Hanna NH et al. **Phase III trial of cisplatin (P) plus etoposide (E) plus concurrent chest radiation (XRT) with or without consolidation docetaxel (D) in patients with inoperable stage III non-small cell lung cancer (NSCLC): HOG LUN 01-24/USO-023.** *Proc ASCO* 2007;**Abstract 7512**.

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**

Scagliotti GV et al. **A randomized phase III trial of cisplatin and pemetrexed versus cisplatin and gemcitabine in patients with locally advanced or metastatic non-small cell lung cancer.** *Proc 12th World Conference on Lung Cancer* 2007;**Abstract PRS-03**.

Winton T et al. **Vinorelbine plus cisplatin vs observation in resected non–small-cell lung cancer.** *N Engl J Med* 2005;352:2589-97. **Abstract**

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **ECOG-E4599 evaluated the addition of bevacizumab to paclitaxel/carboplatin as first-line therapy for patients with NSCLC who did not have _____.**
   a. Squamous cell tumors
   b. Brain metastases
   c. History of hemoptysis
   d. All of the above

2. **The INTEREST trial compared gefitinib to docetaxel as second-line therapy for patients with metastatic NSCLC. The efficacy of _____.**
   a. Gefitinib and docetaxel were comparable
   b. Gefitinib was more favorable than that of docetaxel
   c. Docetaxel was more favorable than that of gefitinib

3. **ECOG-E1505 will evaluate adjuvant _____ with or without bevacizumab for patients with completely resected, Stage IB to IIIA NSCLC.**
   a. Cisplatin/gemcitabine
   b. Cisplatin/vinorelbine
   c. Cisplatin/docetaxel
   d. All of the above

4. **HOG LUN 01-24 demonstrated that consolidation therapy with docetaxel improved survival for patients with Stage IIIA/B NSCLC undergoing treatment with cisplatin/etoposide and concurrent radiation therapy.**
   a. True
   b. False

5. **In the AVAiL trial, the addition of _____ to cisplatin/gemcitabine improved progression-free survival for patients with chemotherapy-naïve, advanced or recurrent NSCLC.**
   a. Bevacizumab at 7.5 mg/kg
   b. Bevacizumab at 15 mg/kg
   c. Both a and b

6. **ZD6474 (vandetanib) is an oral _____ tyrosine kinase inhibitor.**
   a. EGFR
   b. VEGFR
   c. Both a and b
   d. None of the above

7. **In a planned subset analysis of a Phase III trial presented by Scagliotti, overall survival was longer with cisplatin/pemetrexed than with cisplatin/gemcitabine among patients with _____.**
   a. Squamous cell carcinoma
   b. Adenocarcinoma or large cell carcinoma
   c. Both a and b
   d. None of the above

8. **In SWOG-S0533, which of the following characteristics defines high-risk status?**
   a. History of hemoptysis
   b. Central tumor location or tumor cavitation
   c. Squamous histology
   d. All of the above

9. **During the induction therapy phase of SWOG-S0533, the three cohorts of patients will receive no bevacizumab, bevacizumab in the middle of induction therapy or bevacizumab at the beginning of induction therapy with cisplatin/etoposide and radiation.**
   a. True
   b. False

10. **The Southwest Oncology Group (SWOG) is currently evaluating the combination of erlotinib and bevacizumab for patients with Stage IIIB/IV NSCLC in _____.**
    a. Patients with BAC or adenocarcinoma with BAC features
    b. Never smokers
    c. Both a and b

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

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Lung Cancer Update — Issue 1, 2008

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 = Expert 3 = Above average 2 = Competent 1 = Insufficient

Selection of chemotherapy for the treatment of NSCLC in the adjuvant setting. 4 3 2 1
Clinical trials evaluating biologic agents for the treatment of NSCLC in the adjuvant setting 4 3 2 1
Incorporating biologics into the treatment algorithm in the metastatic setting 4 3 2 1
Identifying predictors of response to EGFR inhibitors. 4 3 2 1

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

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

Selection of chemotherapy for the treatment of NSCLC in the adjuvant setting. 4 3 2 1
Clinical trials evaluating biologic agents for the treatment of NSCLC in the adjuvant setting 4 3 2 1
Incorporating biologics into the treatment algorithm in the metastatic setting 4 3 2 1
Identifying predictors of response to EGFR inhibitors. 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:

- Describe the key clinical and pathologic risk factors that influence clinician selection of the medical and surgical management of lung cancer. . . . . 4 3 2 1 N/M N/A
- Develop an evidence-based algorithm for the initial treatment of localized non-small cell lung cancer (NSCLC), exploring the roles of neoadjuvant and adjuvant systemic therapy. . . . . 4 3 2 1 N/M N/A
- Discuss the existing data and emerging research focusing on the optimal management of locally advanced Stage III NSCLC, incorporating the concepts of induction chemotherapy, concomitant chemoradiation therapy and the role of consolidation regimens. . . . . 4 3 2 1 N/M N/A
- Review the existing research that supports alternative doses, formulations and schedules of the commonly used adjuvant and metastatic chemotherapeutic regimens. . . . . 4 3 2 1 N/M N/A
- Describe the emerging role of novel taxane delivery systems and associated efficacy and tolerability findings. . . . . 4 3 2 1 N/M N/A
- Review and critique the emerging clinical research data and ongoing trials evaluating the future roles of novel molecular targeted agents in lung cancer. . . . . 4 3 2 1 N/M N/A
- Describe the contributory roles of surgery, radiation therapy (local and prophylactic cranial irradiation) and chemotherapy in the management of limited- and/or extensive-stage SCLC. . . . . 4 3 2 1 N/M N/A
- Counsel appropriately selected patients about the availability of ongoing clinical trial participation. . . . . 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:

.....

.....

May we include you in future assessments to evaluate the effectiveness of this activity?

☐ Yes ☐ No

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

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

Faculty	Knowledge of subject matter	Effectiveness as an educator
Paul A Bunn Jr, MD	4 3 2 1	4 3 2 1
Nasser H Hanna, MD	4 3 2 1	4 3 2 1
Antoinette J Wozniak, MD	4 3 2 1	4 3 2 1

Please recommend additional faculty for future activities:

.....

Other comments about the faculty for this activity:

.....

REQUEST FOR CREDIT — Please print clearly

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

Degree:

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

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

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Lung Cancer™ UPDATE

This program is supported by educational grants from Abraxis BioScience, AstraZeneca Pharmaceuticals LP, Genentech BioOncology/ OSI Pharmaceuticals Inc and Sanofi-Aventis.

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Last review date: February 2008
Release date: February 2008
Expiration date: February 2009
Estimated time to complete: 3 hours