Consensus or Controversy: Clinical Investigators Provide Their Perspectives on Practical Issues and Research Questions in the Management of Non-Small Cell Lung Cancer

TARGET AUDIENCE

This activity is intended for medical oncologists, hematology-oncology fellows and other healthcare providers involved in the treatment of non-small cell lung cancer (NSCLC).

OVERVIEW OF ACTIVITY

Lung cancer is a devastating disease with a broad-reaching impact on public health, accounting for 15% of all new cancer cases in the United States and the most cancer-related deaths among both men and women. Development of new therapeutic strategies beyond cytotoxic chemotherapy has been the focus of extensive recent research and has led to an explosion in lung cancer genetic and biologic knowledge. The advent of these next-generation targeted treatments presents new promise of both efficacy and enhanced safety for patients with lung cancer but also challenges practicing oncologists to appropriately select individuals who may benefit from these agents and to determine how to integrate such therapies, as they become available, into standard lung cancer treatment algorithms. Several consensus- and evidence-based treatment guidelines are available and aim to assist clinicians with making lung cancer management decisions in the face of this dynamic clinical environment, but despite the existence of these tools, many areas of controversy persist within academic and community settings. This program uses a review of recent relevant publications and other relevant presentations, ongoing clinical trials and Q&A to assist medical oncologists, hematology-oncology fellows and other healthcare providers with the formulation of up-to-date clinical management strategies, including referral of appropriate patients to ongoing pivotal clinical trials.

LEARNING OBJECTIVES

- Develop an evidence-based strategy for the initial diagnosis and treatment of localized NSCLC, exploring the role of neoadjuvant and adjuvant systemic therapy.
- Use biomarkers, clinical characteristics and tumor histology to select individualized front-line and subsequent treatment approaches for patients with metastatic NSCLC.
- Compare and contrast the benefits and risks of combination chemobiologic, doublet and single-agent chemotherapy regimens when developing treatment plans for patients with advanced NSCLC.
- Recognize the effect of NSCLC tumor-specific mutations on relative response or resistance to treatment with EGFR TKIs, monoclonal antibodies and other emerging molecular-targeted agents.
- Identify patients with metastatic NSCLC who may experience clinical benefit from the addition of continuation or switch maintenance biologic therapy and/or chemotherapy.
- Recall the design of ongoing clinical trials evaluating novel investigational agents in NSCLC, and counsel appropriately selected patients about availability and participation.

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FACULTY — 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:

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Hardware/Software Requirements:
An Internet connection that is at least 28.8 Kbps
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 6.x or newer, Firefox 2.x or newer, or Safari 2.x or newer
Macromedia Flash plug-in 6.0 or greater
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Track 1 Introduction: Dr Love

Track 2 Review of audience polling results — ROS1 tumor translocation and responsiveness to crizotinib

Track 3 Forecast on the expanding roles of driver mutations and immune modulators in treatment selection for patients with non-small cell lung cancer (NSCLC)

Track 4 Faculty and audience poll: In which patients with metastatic NSCLC with tissue already accessed would you order EGFR or ALK testing?

Track 5 Faculty and audience poll: Outside of a clinical trial setting, do you believe there is a role for K-ras testing?

Track 6 Module 1, Dr Langer: Emerging implications of histology and molecular diagnostics in advanced NSCLC

Track 7 Current clinical implications of histopathologic diagnosis for systemic treatment decision-making — Squamous versus nonsquamous versus mixed adenosquamous

Track 8 K-ras: Investigational agents and perspective on current treatment approach

Track 9 Audience-generated question: Is blood-streaked sputum an absolute contraindication for administering bevacizumab?

Track 10 Faculty and audience poll: What would be your initial treatment for a 60-year-old minimally symptomatic patient with EGFR and ALK wild-type metastatic adenocarcinoma without bevacizumab contraindications?

Track 11 Faculty and audience poll: What maintenance treatment, if any, would you choose if the patient experienced a partial response (PR) to initial therapy?

Track 12 Faculty and audience poll: What is your immediate next treatment approach for a 60-year-old patient with metastatic adenocarcinoma who has received 2 cycles of carboplatin/paclitaxel/bevacizumab and whose EGFR test then returns positive for an exon 21 mutation?

Track 13 Module 2, Dr Socinski: Treatment for patients with EGFR wild-type nonsquamous NSCLC

Track 14 Faculty and audience poll: What are some later-line treatment options for a 60-year-old with progressive disease?

Track 15 Audience-generated question: Which chemotherapy is best for patients with K-ras mutation-positive NSCLC?

Track 16 Perspectives on efficacy and side effects of maintenance therapy in NSCLC

Track 17 Faculty and audience poll: What is the optimal treatment for a 60-year-old with slow but definite tumor progression on erlotinib?

Track 18 Faculty and audience poll: What initial therapy would you recommend for a 60-year-old patient with symptomatic EGFR mutation-positive disease but no bevacizumab contraindications?

Track 19 Faculty and audience poll: Should you do a lung biopsy for mutational analysis on an 88-year-old nonsmoker with bone pain and lung and bone metastases?

Track 20 Module 3, Dr Lynch: Treatment decision-making for patients with EGFR mutations, EML4-ALK translocations or ROS rearrangement

Track 21 Faculty and audience poll: What initial treatment strategy would you recommend for a 60-year-old patient with symptomatic EML4-ALK-positive disease and no bevacizumab contraindications?

Track 22 Audience-generated question: What are your thoughts on the spectrum of EGFR mutations, treatment for brain metastases and adjuvant erlotinib?

Track 23 Faculty and audience poll: What first-line chemotherapy regimen do you generally recommend for patients with metastatic squamous cell NSCLC?

Track 24 Module 4, Dr Sequist: Current and future management of advanced squamous cell NSCLC

Track 25 Audience-generated question: What are your thoughts on the risks of core biopsy, circulating tumor cells and driver mutations in small cell lung cancer?

Track 26 Audience-generated question: Where are we with the use of *nab* paclitaxel in squamous cell NSCLC?

Track 27 Audience-generated question: What are the data to support the use of erlotinib beyond progression?

Track 28 Faculty and audience poll: What is your preferred adjuvant treatment regimen for a 60- or 75-year-old with EGFR wild-type adenocarcinoma and 3 positive hilar nodes?

Track 29 Module 5, Dr Soria: Adjuvant treatment for NSCLC

Track 30 Audience-generated question: Should you rebiopsy after progression on erlotinib in a patient with EGFR mutation-positive adenocarcinoma and bone metastases?

Track 31 Audience-generated question: What treatment approach would the faculty recommend for a patient with ALK mutation-positive disease experiencing progression on crizotinib?

Track 32 Audience-generated question: What are your perspectives on VeriStrat®?

Track 33 Audience-generated question: What other important data sets will be presented at ASCO 2012 specific to NSCLC?

SELECT PUBLICATIONS

Barlesi F et al. **AVAPERL (MO22089): Final efficacy outcomes for patients (pts) with advanced non-squamous non-small cell lung cancer (nsNSCLC) randomised to continuation maintenance (mtc) with bevacizumab (bev) or bev+pemetrexed (pem) after first-line (1L) bev-cisplatin (cis)-pem treatment (Tx).** *Proc EMCC* 2011. No abstract available

Choi YL et al. **EML4-ALK mutations in lung cancer that confer resistance to ALK inhibitors.** *N Engl J Med* 2010;363(18):1734-9. **Abstract**

D'Angelo SP et al. **Incidence of EGFR exon 19 deletions and L858R in tumor specimens from men and cigarette smokers with lung adenocarcinomas.** *J Clin Oncol* 2011;29(15):2066-70. **Abstract**

Douillard JY et al. **Adjuvant cisplatin and vinorelbine for completely resected non-small cell lung cancer: Subgroup analysis of the Lung Adjuvant Cisplatin Evaluation.** *J Thorac Oncol* 2010;5(2):220-8. **Abstract**

Groen HJ et al. **Activity and tolerability of combined EGFR targeting with afatinib (BIBW 2992) and cetuximab in T790M+ NSCLC patients.** *Proc IASLC* 2011. No abstract available

Haugsten EM et al. **Roles of fibroblast growth factor receptors in carcinogenesis.** *Mol Cancer Res* 2010;8(11):1439-52. **Abstract**

Johnson DH et al. **Randomized phase II trial comparing bevacizumab plus carboplatin and paclitaxel with carboplatin and paclitaxel alone in previously untreated locally advanced or metastatic non-small-cell lung cancer.** *J Clin Oncol* 2004;22(11):2184-91. **Abstract**

Kreuter M et al. **Randomized phase II trial on refinement of early-stage NSCLC adjuvant chemotherapy with cisplatin and pemetrexed (CPx) versus cisplatin and vinorelbine (CVb): TREAT.** *Proc ASCO* 2011;**Abstract 7002**.

Manegold C et al. **Randomised, 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 LBA7515**.

Open-label study of bevacizumab maintenance therapy (AVASTIN®) with or without pemetrexed after first-line chemotherapy with bevacizumab-cisplatin-pemetrexed in patients with advanced, metastatic or recurrent non-squamous non-small cell lung cancer (NSCLC). NCT00961415

Paz-Ares LG et al. **PARAMOUNT: Phase III study of maintenance pemetrexed (pem) plus best supportive care (BSC) versus placebo plus BSC immediately following induction treatment with pem plus cisplatin for advanced nonsquamous non-small cell lung cancer (NSCLC).** *Proc ASCO* 2011;**Abstract CRA7510**.

A Phase III randomized trial of adjuvant chemotherapy with or without bevacizumab for patients with completely resected Stage IB (> 4cm)-IIIA non-small lung cancer (NSCLC). NCT00324805

Pignon JP et al. **Lung adjuvant cisplatin evaluation: A pooled analysis by the LACE Collaborative Group.** *J Clin Oncol* 2008;26(21):3552-9. **Abstract**

Pirker R et al. **EGFR expression as a predictor of survival for first-line chemotherapy plus cetuximab in patients with advanced non-small-cell lung cancer: Analysis of data from the phase 3 FLEX study.** *Lancet Oncol* 2012;13(1):33-42. **Abstract**

Pirker R et al. **Cetuximab plus chemotherapy in patients with advanced non-small-cell lung cancer (FLEX): An open-label randomised phase III trial.** *Lancet* 2009;373(9674):1525-31. **Abstract**

Randomized, open-label, Phase 3 study of pemetrexed plus carboplatin and bevacizumab followed by maintenance pemetrexed and bevacizumab versus paclitaxel plus carboplatin and bevacizumab followed by maintenance bevacizumab in patients with Stage IIIB or IV nonsquamous non-small cell lung cancer. NCT00762034

Randomized Phase III study of maintenance therapy with bevacizumab, pemetrexed, or a combination of bevacizumab and pemetrexed following carboplatin, paclitaxel and bevacizumab for advanced non-squamous NSCLC. NCT01107626

Reck M et al. **Phase III trial of cisplatin plus gemcitabine with either placebo or bevacizumab as first-line therapy for nonsquamous non-small-cell lung cancer: AVAil.** *J Clin Oncol* 2009;27(8):1227-34. **Abstract**

Regales L et al. **Dual targeting of EGFR can overcome a major drug resistance mutation in mouse models of EGFR mutant lung cancer.** *J Clin Invest* 2009;119(10):3000-10. **Abstract**

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. **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**

Soda M et al. **Identification of the transforming EML4-ALK fusion gene in non-small-cell lung cancer.** *Nature* 2007;448(7153):561-6. **Abstract**

Yu J et al. **Detecting EGFR mutations in NSCLC by immunohistochemistry.** ASCO Molecular Markers 2008;**Abstract 64**.

Zhu J et al. **Carboplatin and paclitaxel with vs without bevacizumab in older patients with advanced non-small cell lung cancer.** *JAMA* 2012;307(15):1593-601. **Abstract**