

Proceedings from the 12th Annual Winter Lung Cancer Conference

CME Information

TARGET AUDIENCE

This educational activity has been designed to meet the educational needs of medical oncologists, hematology-oncology fellows, nurse practitioners and other allied cancer professionals involved in the treatment of lung cancer.

OVERVIEW OF ACTIVITY

Lung cancer is a devastating disease that accounts for approximately 13% of new cancer cases and more cancer-related deaths among both men and women than any other tumor type. In the year 2015, it is estimated that 221,200 individuals will be diagnosed and 158,040 individuals will die from the disease. The plethora of available cytotoxic chemotherapies exhibiting activity in lung cancer has increased substantially over the past several years, and 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.

This unique educational activity delivers highly applicable current clinical information delving into the personalized management of this challenging disease and provides clinicians with a concise, easy-to-understand resource to facilitate knowledge and application of optimal diagnostic and therapeutic approaches.

LEARNING OBJECTIVES

- Develop an evidence-based strategy for the treatment of localized non-small cell lung cancer (NSCLC), exploring the role of (neo)adjuvant systemic therapy.
- Employ an understanding of personalized medicine to individualize the use of available EGFR inhibitors in the treatment of NSCLC.

- Describe mechanisms of tumor resistance to EGFR tyrosine kinase inhibitors, and identify therapeutic opportunities to circumvent this process.
- Communicate the efficacy and safety of crizotinib, ceritinib and other emerging ALK inhibitors to appropriate patients with NSCLC, considering the predictive utility of ALK and ROS1 mutation testing.
- Devise an evidence-based approach to the selection of induction and maintenance biologic therapy and/or chemotherapy for patients with advanced pan-wild-type NSCLC.
- Describe emerging data on the efficacy and safety of tumor immunotherapy in lung cancer, and consider this information when counseling patients regarding clinical trial participation.
- Assess new oncogenic pathways mediating the growth of unique NSCLC tumor subsets, and recall emerging data with experimental agents exploiting these targets.
- Formulate management strategies for small cell lung cancer, considering the contributory roles of local and systemic therapy.
- Consider the use of multimodality therapy for appropriate patients with mesothelioma who may potentially be cured with this approach.
- Recall the design of ongoing clinical trials evaluating novel investigational agents in lung cancer, and counsel appropriately selected patients about availability and participation.

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A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

Last review date: June 2015

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Select Publications

Keynote: Small Cell Lung Cancer — Where Do We Go From Here?

Charles M Rudin, MD, PhD

A multi-center, randomized, double-blind phase II study comparing ABT-888, a PARP inhibitor, versus placebo with temozolomide in patients with relapsed sensitive or refractory small cell lung cancer. NCT01638546

A phase 1b/2 study of OMP-59R5 in combination with etoposide and platinum therapy in subjects with untreated extensive stage small cell lung cancer (PINNACLE). NCT01859741

Belani CP et al. **Three-arm randomized phase II study of cisplatin and etoposide (CE) versus CE with either vismodegib (V) or cixutumumab (Cx) for patients with extensive stage-small cell lung cancer (ES-SCLC) (ECOG 1508).** *Proc ASCO* 2013;Abstract 7508.

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Gandhi L et al. **Phase I study of navitoclax (ABT-263), a novel Bcl-2 family inhibitor, in patients with small-cell lung cancer and other solid tumors.** *J Clin Oncol* 2011;29(7):909-16.

Gardner EE et al. **Rapamycin rescues ABT-737 efficacy in small cell lung cancer.** *Cancer Res* 2014;74(10):2846-56.

Han CL et al. **Therapeutic efficacy of ABT-737, a selective inhibitor of BCL-2, in small cell lung cancer.** *Cancer Res* 2008;68(7):2321-8.

Hanna N et al. **Randomized phase III trial comparing irinotecan/cisplatin with etoposide/cisplatin in patients with previously untreated extensive-stage disease small-cell lung cancer.** *J Clin Oncol* 2006;24(13):2038-43.

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Jahchan NS et al. **A drug repositioning approach identifies tricyclic antidepressants as inhibitors of small cell lung cancer and other neuroendocrine tumors.** *Cancer Discov* 2013;3(12):1364-77.

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Slotman B et al. **Prophylactic cranial irradiation in extensive small-cell lung cancer.** *N Engl J Med* 2007;357(7):664-72.

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Module 1: EGFR Mutation-Positive Disease

Charles M Rudin, MD, PhD

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Kwak EL et al. **Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer.** *N Engl J Med* 2010;363(18):1693-703.

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Roy S Herbst, MD, PhD

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Leora Horn, MD, MSc

A phase III randomised, double blind, placebo controlled, parallel, multicentre study to assess the efficacy and safety of continuing IRESSA 250 mg in addition to chemotherapy versus chemotherapy alone in patients who have epidermal growth factor receptor (EGFR) mutation positive locally advanced or metastatic non-small cell lung cancer (NSCLC) and have progressed on first line IRESSA. NCT01544179

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Pao W et al. **Acquired resistance of lung adenocarcinomas to gefitinib or erlotinib is associated with a second mutation in the EGFR kinase domain.** *PLoS Med* 2005;2(3):e73.

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Julie R Brahmer, MD

A phase 1/2, open-label, safety, pharmacokinetic and preliminary efficacy study of oral rociletinib in patients with previously treated mutant EGFR non-small cell lung cancer (NSCLC). NCT01526928

AURA: Safety, tolerability, pharmacokinetics and anti-tumour activity of AZD9291 in patients with advanced non-small cell lung cancer who progressed on prior therapy with an epidermal growth factor receptor tyrosine kinase inhibitor agent. NCT01802632

AURA2: Phase II, open label, single-arm study to assess safety and efficacy of AZD9291 in patients with locally advanced/metastatic NSCLC whose disease has progressed with previous EGFR TKI and whose tumours are EGFR and T790M mutation positive. NCT02094261

AURA3: A phase III, open label, randomized study of AZD9291 versus platinum-based doublet chemotherapy for patients with locally advanced or metastatic non-small cell lung cancer whose disease has progressed with previous epidermal growth factor receptor tyrosine kinase inhibitor therapy and whose tumours harbour a T790M mutation within the epidermal growth factor receptor gene. NCT02151981

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TIGER 1: A randomized, open-label, phase 2 study of CO-1686 or erlotinib as first-line treatment of patients with EGFR-mutant advanced NSCLC. NCT02186301

TIGER-2: A phase 2, open-label, multicenter, safety and efficacy study of oral CO-1686 as 2nd-line EGFR-directed TKI in patients with mutant EGFR non-small cell lung cancer (NSCLC). NCT02147990

TIGER-3: A phase 3, open-label, multicenter, randomized study of oral rociletinib (CO-1686) monotherapy versus single-agent cytotoxic chemotherapy in patients with mutant EGFR non-small cell lung cancer (NSCLC) after failure of at least 1 previous EGFR-directed tyrosine kinase inhibitor (TKI) and platinum-doublet chemotherapy. NCT02322281

Module 2: EML4-ALK, ROS1 and Other Potentially Targetable Mutations

David E Gerber, MD

ALEX: A randomized, multicenter, phase III, open-label study of alectinib versus crizotinib in treatment-naive anaplastic lymphoma kinase-positive advanced non-small cell lung cancer. NCT02075840

Atherly AJ, Camidge DR. **The cost-effectiveness of screening lung cancer patients for targeted drug sensitivity markers.** *Br J Cancer 2012;106(6):1100-6.*

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Davies KD et al. **Identifying and targeting ROS1 gene fusions in non-small cell lung cancer.** *Clin Cancer Res 2012;18(17):4570-9.*

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Ren S et al. **Atypical negative ALK break-apart FISH harboring a crizotinib-responsive ALK rearrangement in non-small-cell lung cancer.** *J Thorac Oncol* 2014;9(3):e21-3.

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Sang J et al. **Targeted inhibition of the molecular chaperone HSP90 overcomes ALK inhibitor resistance in non-small cell lung cancer.** *Cancer Discov* 2013;3(4):430-43.

Sasaki T et al. **A novel ALK secondary mutation and EGFR signaling cause resistance to ALK kinase inhibitors.** *Cancer Res* 2011;71(18):6051-60.

Sequist LV et al. **Activity of IPI-504, a novel heat-shock protein 90 inhibitor, in patients with molecularly defined non-small-cell lung cancer.** *J Clin Oncol* 2010;28(33):4953-60.

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Ramaswamy Govindan, MD

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NCT00409968

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NCT02154490

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Module 3: Immune Checkpoint Inhibitors

Leora Horn, MD, MSc

Antonia SJ et al. **A Phase I open-label study to evaluate the safety and tolerability of MEDI4736, an anti-programmed cell death-ligand 1 (PD-L1) antibody, in combination with tremelimumab in patients with advanced non-small cell lung cancer (NSCLC).** *Proc ESMO* 2014;Abstract 1327P.

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McDermott DF et al. **Immune correlates and long term follow up of a phase Ia study of MPDL3280A, an engineered PD-L1 antibody, in patients with metastatic renal cell carcinoma (mRCC).** *Proc ESMO* 2014;Abstract 8090.

Ramalingam SS et al. **Phase II study of nivolumab (anti-PD-1, BMS-936558, ONO-4538) in patients with advanced, refractory squamous non-small cell lung cancer.** *Int J Radiat Oncol Biol Phys* 2014;90(5):1266-7.

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Julie R Brahmer, MD

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Herbst RS et al. **Predictive correlates of response to the anti-PD-L1 antibody MPDL3280A in cancer patients.** *Nature* 2014;515(7528):563-7.

Hochstrasser A et al. **Interstitial pneumonitis after treatment with pemetrexed: A rare event?** *Chemotherapy* 2012;58(1):84-8.

Inoue A et al. **Radiation pneumonitis in lung cancer patients: A retrospective study of risk factors and the long-term prognosis.** *Int J Radiat Oncol Biol Phys* 2001;49(3):649-55.

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Roychowdhury DF et al. **A report on serious pulmonary toxicity associated with gemcitabine-based therapy.** *Invest New Drugs* 2002;20(3):311-5.

Topalian SL et al. **Safety, activity, and immune correlates of anti-PD-1 antibody in cancer.** *N Engl J Med* 2012;366(26):2443-54.

Roy S Herbst, MD, PhD

A phase 1, open-label, multicenter, safety study of nivolumab (BMS-936558) in combination with *nab*-paclitaxel plus or minus gemcitabine in pancreatic cancer, *nab*-paclitaxel/carboplatin in stage IIIB/IV non-small cell lung cancer or *nab*-paclitaxel in recurrent metastatic breast cancer. NCT02309177

A phase 1b, open-label, multicenter, multidose, dose-escalation study of MDX-1106 in subjects with selected advanced or recurrent malignancies. NCT00730639

A phase I, open-label, multicentre study to assess the safety, tolerability, pharmacokinetics and preliminary anti-tumour activity of gefitinib in combination with MEDI4736 (anti PD-L1) in subjects with non-small cell lung cancer (NSCLC). NCT02088112

Antonia SJ et al. **A Phase I open-label study to evaluate the safety and tolerability of MEDI4736, an anti-programmed cell death-ligand 1 (PD-L1) antibody, in combination with tremelimumab in patients with advanced non-small cell lung cancer (NSCLC).** *Proc ESMO* 2014;Abstract 1327P.

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Antonia SJ et al. **Nivolumab (anti-PD-1; BMS-936558, ONO-4538) in combination with platinum-based doublet chemotherapy (PT-DC) in advanced non-small cell lung cancer (NSCLC).** *Proc ASCO* 2014;Abstract 8113.

Antonia S et al. **Association of tumor PD-L1 expression and immune biomarkers with clinical activity in patients with non-small cell lung cancer (NSCLC) treated with nivolumab (anti-PD-1; BMS-936558; ONO-4538).** *Proc WCLC* 2013;Abstract P2.11-035.

ARCTIC : A phase III, open label, randomised, multi-centre, international study of MEDI4736, given as monotherapy or in combination with tremelimumab determined by PD-L1 expression versus standard of care in patients with locally advanced or metastatic non-small cell lung cancer (Stage IIIB-IV) who have received at least two prior systemic treatment regimens including one platinum based chemotherapy regimen and do not have known EGFR TK activating mutations or ALK rearrangements. NCT02352948

CheckMate 012: A multi-arm phase I safety study of nivolumab in combination with gemcitabine/cisplatin, pemetrexed/ cisplatin, carboplatin/paclitaxel, bevacizumab maintenance, erlotinib, ipilimumab or as monotherapy in subjects with stage IIIB/ IV non-small cell lung cancer (NSCLC). NCT01454102

CheckMate 063: A single-arm phase 2 study of nivolumab (BMS-936558) in subjects with advanced or metastatic squamous cell non-small cell lung cancer who have received at least two prior systemic regimens. NCT01721759

Garon EB et al. **Antitumor activity of pembrolizumab (Pembro; MK-3475) and correlation with programmed death ligand 1 (PD-L1) expression in a pooled analysis of patients (pts) with advanced non-small cell lung carcinoma (NSCLC).** *Proc ESMO* 2014;Abstract LBA43.

Herbst RS et al. **Predictive correlates of response to the anti-PD-L1 antibody MPDL3280A in cancer patients.** *Nature* 2014;515(7528):563-7.

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KEYNOTE-001: Phase I study of single agent MK-3475 in patients with progressive locally advanced or metastatic carcinoma, melanoma, and non-small cell lung carcinoma. NCT01295827

KEYNOTE-021: A phase I/II study of MK-3475 (SCH900475) in combination with chemotherapy or immunotherapy in patients with locally advanced or metastatic non-small cell lung carcinoma. NCT02039674

Mellman I et al. **Cancer immunotherapy comes of age.** *Nature* 2011;480(7378):480-9.

Powderly JD et al. **Biomarkers and associations with the clinical activity of PD-L1 blockade in a MPDL3280A study.** *Proc ASCO* 2013;Abstract 3001.

Ramalingam SS et al. **Phase II study of nivolumab (anti-PD-1, BMS-936558, ONO-4538) in patients with advanced, refractory squamous non-small cell lung cancer.** *Int J Radiat Oncol Biol Phys* 2014;90(5):1266-7.

Rizvi NA et al. **Safety and response with nivolumab (anti-PD-1; BMS-936558, ONO-4538) plus erlotinib in patients (pts) with epidermal growth factor receptor mutant (EGFR MT) advanced NSCLC.** *Proc ASCO* 2014;Abstract 8022.

Velcheti V et al. **Programmed death ligand-1 expression in non-small cell lung cancer.** *Lab Invest* 2014;94(1):107-16.

Module 4: Lung Cancer Research and Practice in the General Oncology Setting

Mark A Socinski, MD

A randomized, phase III study comparing carboplatin/paclitaxel or carboplatin/paclitaxel/bevacizumab with or without concurrent cetuximab in patients with advanced non-small cell lung cancer (NSCLC). NCT00946712

ATLAS: A randomized, double-blind, placebo-controlled, phase IIIb trial comparing bevacizumab therapy with or without erlotinib after completion of chemotherapy with bevacizumab for the first-line treatment of locally advanced, recurrent, or metastatic non-small cell lung cancer. NCT00257608

Fuchs CS et al. **Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): An international, randomised, multicentre, placebo-controlled, phase 3 trial.** *Lancet* 2014;383(9911):31-9.

Garon EB et al. **Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): A multicentre, double-blind, randomised phase 3 trial.** *Lancet* 2014;384(9944):665-73.

Gregorc V et al. **Predictive value of a proteomic signature in patients with non-small-cell lung cancer treated with second-line erlotinib or chemotherapy (PROSE): A biomarker-stratified, randomised phase 3 trial.** *Lancet Oncol* 2014;15(7):713-21.

Hensing TA et al. **Factors associated with the likelihood of receiving second line therapy for advanced non-small cell lung cancer.** *Lung Cancer* 2005;47(2):253-9.

JMEN: A phase 3, double-blind, placebo-controlled study of maintenance pemetrexed plus best supportive care versus best supportive care immediately following induction treatment for advanced non-small cell lung cancer. NCT00102804

Lee JK et al. **Epidermal growth factor receptor tyrosine kinase inhibitors vs conventional chemotherapy in non-small cell lung cancer harboring wild-type epidermal growth factor receptor: A meta-analysis.** *JAMA* 2014;311(14):1430-7.

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

SATURN: Erlotinib (Tarceva) in routine clinical practice for first line maintenance therapy (1LM) in patients with advanced non-small cell lung cancer (NSCLC). NCT01194050

Socinski MA et al. **Phase III trial comparing a defined duration of therapy versus continuous therapy followed by second-line therapy in advanced-stage IIIB/IV non-small-cell lung cancer.** *J Clin Oncol* 2002;20(5):1335-43.

Stinchcombe TE et al. **A retrospective analysis of VeriStrat status on outcome of a randomized phase II trial of first-line therapy with gemcitabine, erlotinib, or the combination in elderly patients (age 70 years or older) with stage IIIB/IV non-small-cell lung cancer.** *J Thorac Oncol* 2013;8(4):443-51.

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Ramaswamy Govindan, MD

Brahmer JR et al. **Clinical activity and biomarkers of MEDI4736, an anti-PD-L1 antibody, in patients with NSCLC.** *Proc ASCO* 2014;Abstract 8021.

Brahmer J et al. **Survival and long-term follow-up of the phase I trial of nivolumab (anti-PD-1; BMS-936558; ONO-4538) in patients (pts) with previously treated advanced non-small cell lung cancer (NSCLC).** *Proc ASCO* 2013;Abstract 8030.

Cancer Genome Atlas Research Network. **Comprehensive genomic characterization of squamous cell lung cancers.** *Nature* 2012;489(7417):519-25.

Goss G et al. **A randomized, open-label, phase III trial of afatinib (A) vs erlotinib (E) as second-line treatment of patients (pts) with advanced squamous cell carcinoma (SCC) of the lung following first-line platinum-based chemotherapy: LUX-Lung 8 (LL8).** *Proc ESMO* 2014;Abstract 12220.

Hirsh V et al. **Patient-reported neuropathy and taxane-associated symptoms in a phase 3 trial of nab-paclitaxel plus carboplatin versus solvent-based paclitaxel plus carboplatin for advanced non-small-cell lung cancer.** *J Thorac Oncol* 2014;9(1):83-90.

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Spigel DR et al. **Clinical activity, safety, and biomarkers of MPDL3280A, an engineered PD-L1 antibody in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC).** *Proc ASCO* 2013;Abstract 8008.

Thatcher N et al. **A randomized, multicenter, open-label, phase III study of gemcitabine-cisplatin (GC) chemotherapy plus necitumumab (IMC-11F8/LY3012211) versus GC alone in the first-line treatment of patients (pts) with stage IV squamous non-small cell lung cancer (sq-NSCLC).** *Proc ASCO* 2014;Abstract 8008.

Wu YM et al. **Identification of targetable FGFR gene fusions in diverse cancers.** *Cancer Discov* 2013;3(6):636-47.

Roy S Herbst, MD, PhD

A phase III double-blind trial for surgically resected early stage non-small cell lung cancer: Crizotinib versus placebo for patients with tumors harboring the anaplastic lymphoma kinase (ALK) fusion protein (an ALCHEMIST treatment trial). NCT02201992

Adjuvant lung cancer enrichment marker identification and sequencing trial (ALCHEMIST). NCT02194738

Lung-MAP: S1400 phase II/III biomarker-driven master protocol for second line therapy of squamous cell lung cancer. NCT02154490

Randomized double blind placebo controlled study of erlotinib or placebo in patients with completely resected epidermal growth factor receptor (EGFR) mutant non-small cell lung cancer (NSCLC) (an ALCHEMIST treatment trial). NCT02193282

Rogerio C Lilenbaum, MD

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Module 5: Management of Mesothelioma; Surgical Issues; Treatment of Brain Metastases

Harvey I Pass, MD

Flores RM et al. **Extrapleural pneumonectomy versus pleurectomy/decortication in the surgical management of malignant pleural mesothelioma: Results in 663 patients.** *J Thorac Cardiovasc Surg* 2008;135(3):620-6.

Gill RR et al. **Epithelial malignant pleural mesothelioma after extrapleural pneumonectomy: Stratification of survival with CT-derived tumor volume.** *AJR Am J Roentgenol* 2012;198(2):359-63.

Pass HI et al. **Supplementary prognostic variables for pleural mesothelioma: A report from the IASLC staging committee.** *J Thorac Oncol* 2014;9(6):856-64.

Pass HI et al. **Preoperative tumor volume is associated with outcome in malignant pleural mesothelioma.** *J Thorac Cardiovasc Surg* 1998;115(2):310-7.

Rice D et al. **Recommendations for uniform definitions of surgical techniques for malignant pleural mesothelioma: A consensus report of the international association for the study of lung cancer international staging committee and the international mesothelioma interest group.** *J Thorac Oncol* 2011;6(8):1304-12.

Rusch VW et al. **Initial analysis of the international association for the study of lung cancer mesothelioma database.** *J Thorac Oncol* 2012;7(11):1631-9.

Treasure T et al. **Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: Clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study.** *Lancet Oncol* 2011;12(8):763-72.

Everett E Vokes, MD

Calabrò L et al. **CTLA4 blockade in mesothelioma: Finally a competing strategy over cytotoxic/target therapy?** *Cancer Immunol Immunother* 2015;64(1):105-12.

Jassem J et al. **Phase III trial of pemetrexed plus best supportive care compared with best supportive care in previously treated patients with advanced malignant pleural mesothelioma.** *J Clin Oncol* 2008;26(10):1698-704.

Nowak AK et al. **A phase II study of intermittent sunitinib malate as second-line therapy in progressive malignant pleural mesothelioma.** *J Thorac Oncol* 2012;7(9):1449-56.

Randomized phase II study of maintenance pemetrexed versus observation for patients with malignant pleural mesothelioma without progression after first-line chemotherapy. NCT01085630

Toyokawa G et al. **Gemcitabine and vinorelbine as second-line or beyond treatment in patients with malignant pleural mesothelioma pretreated with platinum plus pemetrexed chemotherapy.** *Int J Clin Oncol* 2014;19(4):601-6.

van den Bogaert DP et al. **Pemetrexed maintenance therapy in patients with malignant pleural mesothelioma.** *J Thorac Oncol* 2006;1(1):25-30.

Vogelzang NJ et al. **Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma.** *J Clin Oncol* 2003;21(14):2636-44.

Zucali PA et al. **Vinorelbine in pemetrexed-pretreated patients with malignant pleural mesothelioma.** *Lung Cancer* 2014;84(3):265-70.

A William Blackstock, MD

Chang JY et al. **Stereotactic ablative radiation therapy for centrally located early stage or isolated parenchymal recurrences of non-small cell lung cancer: How to fly in a “no fly zone.”** *Int J Radiat Oncol Biol Phys* 2014;88(5):1120-8.

Kilburn JM et al. **Management of mediastinal relapse after treatment with stereotactic body radiotherapy or accelerated hypofractionated radiotherapy for stage I/II non-small-cell lung cancer.** *J Thorac Oncol* 2014;9(4):572-6.

Timmerman R et al. **Stereotactic body radiation therapy for inoperable early stage lung cancer.** *JAMA* 2010;303(11):1070-6.

Joel W Neal, MD, PhD

Gani C et al. **Outcome after whole brain radiotherapy alone in intracranial leptomeningeal carcinomatosis from solid tumors.** *Strahlenther Onkol* 2012;188(2):148-53.

Grommes C et al. **“Pulsatile” high-dose weekly erlotinib for CNS metastases from EGFR mutant non-small cell lung cancer.** *Neuro Oncol* 2011;13(12):1364-9.

Hoffknecht P et al. **Efficacy of the irreversible ErbB family blocker afatinib in epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI)-pretreated non-small-cell lung cancer patients with brain metastases or leptomeningeal disease.** *J Thorac Oncol* 2015;10(1):156-63.

Lee SJ et al. **Leptomeningeal carcinomatosis in non-small-cell lung cancer patients: Impact on survival and correlated prognostic factors.** *J Thorac Oncol* 2013;8(2):185-91.

Lim SH et al. **Randomized phase III trial of stereotactic radiosurgery (SRS) versus observation for patients with asymptomatic cerebral oligo-metastases in non-small cell lung cancer (NSCLC).** *Proc ASCO* 2014;Abstract 8037.

Morris PG et al. **Leptomeningeal metastasis from non-small cell lung cancer: Survival and the impact of whole brain radiotherapy.** *J Thorac Oncol* 2012;7(2):382-5.

Riess JW et al. **Prolonged survival of patients with non-small-cell lung cancer with leptomeningeal carcinomatosis in the modern treatment era.** *Clin Lung Cancer* 2014;15(3):202-6.

Scott BJ et al. **Concurrent intrathecal methotrexate and liposomal cytarabine for leptomeningeal metastasis from solid tumors: A retrospective cohort study.** *J Neurooncol* 2014;119(2):361-8.

Shaw A et al. **Evaluation of ceritinib-treated patients (pts) with anaplastic lymphoma kinase rearranged (ALK+) non-small cell lung cancer (NSCLC) and brain metastases in the ASCEND-1 study.** *Proc ESMO* 2014;Abstract 1293P.

Module 6: Adjuvant and Neoadjuvant Therapy; Locally Advanced Disease

A William Blackstock, MD

A randomized phase II study of individualized combined modality therapy for stage III non-small cell lung cancer (NSCLC). NCT01822496

Bogart JA et al. **Phase I study of accelerated conformal radiotherapy for stage I non-small-cell lung cancer in patients with pulmonary dysfunction: CALGB 39904.** *J Clin Oncol* 2010;28(2):202-6.

Chang JY et al. **Phase 2 study of high-dose proton therapy with concurrent chemotherapy for unresectable stage III nonsmall cell lung cancer.** *Cancer* 2011;117(20):4707-13.

INSPIRE: A multi-national, double-blind, placebo-controlled, randomized, phase III clinical trial of the cancer vaccine Stimuvax® (L-BLP25 or BLP25 liposome vaccine) in Asian subjects with Stage III, unresectable, non-small cell lung cancer (NSCLC) who have demonstrated either stable disease or objective response following primary chemo-radiotherapy. NCT01015443

LucaVax: A double-blind, multicenter, randomized phase III study of the telomerase vaccine, GV1001 administered after curative intent chemo-radiotherapy in patients with inoperable stage III non-small cell lung cancer compared to best supportive care. NCT01579188

Oshiro Y et al. **Results of proton beam therapy without concurrent chemotherapy for patients with unresectable stage III non-small cell lung cancer.** *J Thorac Oncol* 2012;7(2):370-5.

Phase I study of accelerated hypofractionated radiation therapy with concomitant chemotherapy for unresectable Stage III NSCLC. NCT01486602

Randomized phase II trial of individualized adaptive radiotherapy using during-treatment FDG-PET/CT and modern technology in locally advanced non-small cell lung cancer (NSCLC). NCT01507428

START: A multi-center phase III randomized, double-blind placebo-controlled study of the cancer vaccine Stimuvax® (L-BLP25 or BLP25 liposome vaccine) in non-small cell lung cancer (NSCLC) subjects with unresectable Stage III disease. NCT00409188

Mark G Kris, MD

Adjuvant lung cancer enrichment marker identification and sequencing trial (ALCHEMIST). NCT02194738

Chaft JE et al. **Phase II trial of neoadjuvant bevacizumab plus chemotherapy and adjuvant bevacizumab in patients with resectable nonsquamous non-small-cell lung cancers.** *J Thorac Oncol* 2013;8(8):1084-90.

D'Angelo SP et al. **Distinct clinical course of EGFR-mutant resected lung cancers: Results of testing of 1118 surgical specimens and effects of adjuvant gefitinib and erlotinib.** *J Thorac Oncol* 2012;7(12):1815-22.

Hellmann MD et al. **Pathological response after neoadjuvant chemotherapy in resectable non-small-cell lung cancers: Proposal for the use of major pathological response as a surrogate endpoint.** *Lancet Oncol* 2014;15(1):e42-50.

Kelly K et al. **A randomized, double-blind phase 3 trial of adjuvant erlotinib (E) versus placebo (P) following complete tumor resection with or without adjuvant chemotherapy in patients (pts) with stage IB-IIIA EGFR positive (IHC/FISH) non-small cell lung cancer (NSCLC): RADIANT results.** *Proc ASCO* 2014;Abstract 7501.

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Rudin CM. **Dark matter: Defining oncogenic drivers in the epigenome.** *Proc IASLC 2013*;Abstract PL02.2.

Sparano JA et al. **Weekly paclitaxel in the adjuvant treatment of breast cancer.** *N Engl J Med* 2008;358(16):1663-71.

Su S et al. **Patterns of survival and recurrence after surgical treatment of early stage non-small cell lung carcinoma in the ACOSOG Z0030 (ALLIANCE) trial.** *J Thorac Cardiovasc Surg* 2014;147(2):747-53.

Harvey I Pass, MD

Bach PB et al. **Benefits and harms of CT screening for lung cancer: A systematic review.** *JAMA* 2012;307(22):2418-29.

Eguchi T et al. **The new IASLC-ATS-ERS lung adenocarcinoma classification: What the surgeon should know.** *Semin Thorac Cardiovasc Surg* 2014;26(3):210-22.

Flores R et al. **Balancing curability and unnecessary surgery in the context of computed tomography screening for lung cancer.** *J Thorac Cardiovasc Surg* 2014;147(5):1619-26.

Hanna WC, Keshavjee S. **How to follow up patients after curative resection of lung cancer.** *Semin Thorac Cardiovasc Surg* 2013;25(3):213-7.

Ma Z et al. **Does sleeve lobectomy concomitant with or without pulmonary artery reconstruction (double sleeve) have favorable results for non-small cell lung cancer compared with pneumonectomy? A meta-analysis.** *Eur J Cardiothorac Surg* 2007;32(1):20-8.

Manos D et al. **The Lung Reporting and Data System (LU-RADS): A proposal for computed tomography screening.** *Can Assoc Radiol J* 2014;65(2):121-34.

Zhang B et al. **Matched-pair comparisons of stereotactic body radiotherapy (SBRT) versus surgery for the treatment of early stage non-small cell lung cancer: A systematic review and meta-analysis.** *Radiother Oncol* 2014;112(2):250-5.

Rogério C Lilenbaum, MD

Ashworth AB et al. **An individual patient data metaanalysis of outcomes and prognostic factors after treatment of oligometastatic non-small-cell lung cancer.** *Clin Lung Cancer* 2014;15(5):346-55.

Gan GN et al. **Stereotactic radiation therapy can safely and durably control sites of extra-central nervous system oligoprogressive disease in anaplastic lymphoma kinase-positive lung cancer patients receiving crizotinib.** *Int J Radiat Oncol Biol Phys* 2014;88(4):892-8.

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Module 7: Other Practical Issues in the Management of Pan-Wild-Type Metastatic Disease

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