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Illustration by Irin Moore

CLINICAL Lung Cancer

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Perspective

Original Studies

20 Multiple Biomarker Testing Tissue Consumption and Completion Rates With Single-gene Tests and Investigational Use of Oncomine Dx Target Test for Advanced Non—Small-cell Lung Cancer: A Single-center Analysis

Tiffany M. Yu, Carl Morrison, Edward J. Gold, Alison Tradonsky, Andrew J. Layton

The increasing number of genes relevant to non—small-cell lung cancer treatment, combined with small lung tissue samples, has heightened the need for tissue stewardship to enable multiple biomarker testing. The present retrospective analysis evaluated 3659 single-gene tests across 1402 clinician-submitted samples and 169 investigational Oncomine Dx Target Tests. Compared with single-gene testing, the Oncomine Dx Target Test could facilitate successful multiple biomarker testing of small samples.

30 Targeted Tissue and Cell-Free Tumor DNA Sequencing of Advanced Lung Squamous-Cell Carcinoma Reveals Clinically Significant Prevalence of Actionable Alterations

Vincent K. Lam, Hai T. Tran, Kimberly C. Banks, Richard B. Lanman, Waree Rinsurongkawong, Nir Peled, Jeff Lewis, J. Jack Lee, Jack Roth, Emily B. Roarty, Stephen Swisher, AmirAli Talasaz, P. Andrew Futreal, Vassiliki Papadimitrakopoulou, John V. Heymach, Jianjun Zhang

Actionable alterations were identified in 10.5% of patients (primarily by cell-free circulating DNA) from a real-world cohort of primarily advanced-stage lung squamous-cell carcinoma (LUSC). Objective response was observed in all 3 evaluable patients who received targeted therapy. Accurate histopathologic assessment in advanced LUSC can be challenging. Evaluating the genomic landscape in this setting is warranted to potentially identify underappreciated treatment options.

37 Predictors of Distant Failure After Stereotactic Body Radiation Therapy for Stages I to IIA Non—Small-Cell Lung Cancer

Chelsea J. Miller, Brendan Martin, Kyle Stang, Ryan Hutten, Fiori Alite, Christina Small, Bahman Emami, Matthew M. Harkenrider

Stereotactic body radiation therapy (SBRT) is an effective treatment modality for early-stage non—small-cell lung cancer, with excellent rates of local control. Despite this, the predominant pattern of failure in these patients is distant. We sought to identify factors that may help to predict which of these patients are at highest risk of distant failure following SBRT. We retrospectively reviewed 292 patients treated with SBRT for early-stage non—small-cell lung cancer. The primary endpoint was distant failure. We classified patients according to T-stage, tumor size, location and histology, pretreatment positron emission tomography/computed tomography standardized uptake value, smoking status, and age. The 2-year distant failure rate was 22.0%, and the 2-year overall survival was 61.0%. For every 1-year increase in patient age, the hazard of distant failure at any given time was 3% lower (hazard ratio, 0.97; 95% confidence interval, 0.94-0.99; $P = .04$). No other clinical factors emerged as significant predictors, and additional molecular studies may be needed to identify the patients with early-stage lung cancer at highest risk of distant failure.

43 Local Consolidation Therapy (LCT) After First Line Tyrosine Kinase Inhibitor (TKI) for Patients With *EGFR* Mutant Metastatic Non—small-cell Lung Cancer (NSCLC)

Yasir Y. Elamin, Daniel R. Gomez, Mara B. Antonoff, Jacqulyne P. Robichaux, Hai Tran, Melissa K. Shorter, Jadi M. Bohac, Marcelo Vailati Negrao, Xiuning Le, Waree Rinsurogkawong, Jeff Lewis, Lara Lacerda, Emily B. Roarty, Stephen G. Swisher, Jack A. Roth, Jianjun Zhang, Vassiliki Papadimitrakopoulou, John V. Heymach

Despite an initial impressive response to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs), non—small-cell lung cancer (NSCLC) harboring TKI-sensitising EGFR mutations invariably acquire resistance after 9 to 14 months of TKI therapy. We have recently shown that the addition of local consolidation therapy (LCT) with surgery or radiation to standarad of care maintenance therapy improves progression-free survival in patients with molecularly unselected NSCLC. Herein, we retrospectively reviewed patients with EGFR mutant NSCLC treated with first-line TKI and LCT and found that their progression-free survival was 36 months compared with 14 months in patients treated with TKI alone. Our findings suggested that combining LCT with TKI may represent an effective therapeutic startegy in this subset of patients.

Case Report

Available Exclusively Online at www.clinical-lung-cancer.com

e39 Preselection of Lung Cancer Cases Using *FGFR1* mRNA and Gene Copy Number for Treatment With Ponatinib

Terry L. Ng, Hui Yu, Derek E. Smith, Theresa A. Boyle, Emily R. York, Scott Leedy, Dexiang Gao, Dara L. Aisner, Adrie Van Bokhoven, Lynn E. Heasley, Fred R. Hirsch, D. Ross Camidge

A phase 2 biomarker-driven study using epidermal growth factor receptor 1 *FGFR1* gene copy number by silver in-situ hybridization (SISH) and messenger RNA expression by in-situ hybridization (ISH) in lung cancer patients treated with ponatinib was conducted. *FGFR1* ISH and SISH positivity may be associated with a distinct phenotype. Ponatinib's poor tolerance limited the number of patients treated on study.

e53 Stereotactic Ablative Radiotherapy as an Alternative to Lobectomy in Patients With Medically Operable Stage I NSCLC: A Retrospective, Multicenter Analysis

Vieri Scotti, Alessio Bruni, Giulio Francolini, Marco Perna, Polina Vasilyeva, Mauro Loi, Gabriele Simontacchi, Domenico Viggiano, Biancaluisa Lanfranchi, Alessandro Gonfiotti, Juljana Topulli, Emanuela Olmetto, Virginia Maragna, Katia Ferrari, Viola Bonti, Camilla Comin, Sara Balduzzi, Roberto D'Amico, Frank Lohr, Luca Voltolini, Lorenzo Livi

We report the results of a retrospective analysis of 187 patients with stage I to II NSCLC treated with lobectomy or stereotactic body radiation therapy. No significant difference was found in local control, whereas overall survival was significantly better in patients treated with lobectomy. No difference for overall survival was observed between operable patients undergoing stereotactic body radiation therapy and lobectomy.

e63 Five-year Long-term Outcomes of Stereotactic Body Radiation Therapy for Operable Versus Medically Inoperable Stage I Non—small-cell Lung Cancer: Analysis by Operability, Fractionation Regimen, Tumor Size, and Tumor Location

Caitlin A. Schonewolf, Marina Heskel, Abigail Doucette, Sunil Singhal, Melissa A. Frick, Eric P. Xanthopoulos, Michael N. Corradetti, Joseph S. Friedberg, Taine T. Pechet, John P. Christodouleas, William Levin, Abigail Berman, Keith A. Cengel, Vivek Verma, Stephen M. Hahn, John C. Kucharczuk, Ramesh Rengan, Charles B. Simone, II

Stereotactic body radiation therapy is standard for inoperable stage I non—small-cell lung cancer and an emerging surgical alternative in operable patients. Limited long-term data exist according to operability. Analysis of 186 patients (204 lesions) demonstrates stereotactic body radiation therapy is well-tolerated with excellent local control (LC) (5-year LC, 93.7%). Inoperable patients achieved similar LC and cancer-specific survival but worse overall survival, likely owing to comorbidities.

e73 The *KIF5B-RET* Fusion Gene Mutation as a Novel Mechanism of Acquired EGFR Tyrosine Kinase Inhibitor Resistance in Lung Adenocarcinoma

You-cai Zhu, Wen-xian Wang, Qu-xia Zhang, Chun-wei Xu, Wu Zhuang, Kai-qi Du, Gang Chen, Tang-feng Lv, Yong Song

e77 Severe Acute Hepatitis in a Patient Receiving Alectinib for *ALK*-Positive Non—Small-Cell Lung Cancer: Histologic Analysis

Viola W. Zhu, Yuxin Lu, Sai-Hong Ignatius Ou

e81 Efficacy of Local Consolidative Therapy for Oligometastatic Lung Adenocarcinoma Patients Harboring Epidermal Growth Factor Receptor Mutations

Fang Hu, Jianlin Xu, Bo Zhang, Changhui Li, Wei Nie, Ping Gu, Ping Hu, Huimin Wang, Yujun Zhang, Yinchen Shen, Shuyuan Wang, Xueyan Zhang

Evidence on the superiority of local consolidative therapy (LCT) for oligometastatic lung adenocarcinoma patients is scarce. We retrospectively reviewed a total of 231 patients with stage IV lung adenocarcinoma harboring sensitive mutation of epidermal growth factor receptor (EGFR) who received EGFR—tyrosine kinase inhibitor (EGFR-TKI) or EGFR-TKIs plus LCT, and analyzed the progression-free survival (PFS) and overall survival (OS) of the 2 groups. Compared to only EGFR-TKI, LCT improved PFS and overall OS. Survival benefit was regardless of *EGFR* mutation type.

e91 Elective Nodal Irradiation as Adjuvant Radiotherapy for Advanced Thymomas and Thymic Carcinomas

Yeon Joo Kim, Su Ssan Kim, Si Yeol Song, Seung-Il Park, Dong Kwan Kim, Yong-Hee Kim, Hyeong Ryul Kim, Eun Kyung Choi

There are few reports on the field of adjuvant radiotherapy in thymic tumors. We evaluated the clinical outcomes of local radiotherapy and elective nodal irradiation in 47 patients with stage III to IV thymomas or stage II to IV thymic carcinomas. The benefit of elective nodal irradiation seemed not to be predominant over local radiotherapy, so elective nodal irradiation should not be recommended routinely.

e97 Efficacy of Nivolumab and Pembrolizumab in Patients With Advanced Non–Small-Cell Lung Cancer Needing Treatment Interruption Because of Adverse Events: A Retrospective Multicenter Analysis

Doran Ksienski, Elaine S. Wai, Nicole Croteau, Leathia Fiorino, Edward Brooks, Zia Poonja, Dave Fenton, Georiga Geller, Daniel Glick, Mary Lesperance

Nivolumab and pembrolizumab can cause immune-related adverse events (irAE). In this retrospective chart review of advanced non–small-cell lung cancer patients receiving programmed death 1 antibodies in British Columbia, Canada, treatment interruption due to irAE was associated with a lower median overall survival (OS) than those treated continuously. Development of colitis in nivolumab-treated patients was associated with shorter OS than for patients who did not develop colitis.

e107 Lymph Node Size Predicts for Asymptomatic Brain Metastases in Patients With Non–small-cell Lung Cancer at Diagnosis

Stephanie R. Rice, Jason K. Molitoris, Melissa A.L. Vyfhuis, Martin J. Edelman, Whitney M. Burrows, Josephine Feliciano, Elizabeth M. Nichols, Mohan Suntharalingam, James Donahue, Shamus R. Carr, Joseph Friedberg, Shahed Badiyan, Charles B. Simone, II, Steven J. Feigenberg, Pranshu Mohindra

We questioned the National Comprehensive Cancer Network recommendation for staging brain magnetic resonance imaging in patients with stage IB and above non–small-cell lung cancer (NSCLC), and report a 5.7% prevalence of asymptomatic brain metastases in stage I to III NSCLC, with the highest prevalence in lymph node-positive patients. Two stage I patients had asymptomatic brain metastases (adenocarcinoma), whereas no stage II patients had brain metastases, suggesting potential overutilization of brain magnetic resonance imaging staging in this cohort.

e115 Perceptions and Utilization of Lung Cancer Screening Among Smokers Enrolled in a Tobacco Cessation Program

Dan J. Raz, Geena Wu, Rebecca A. Nelson, Virginia Sun, Su Wu, Angel Alem, Eric C. Haupt, Mohamed H. Ismail, Michael K. Gould

Tobacco cessation counseling may be an opportune time to educate about lung cancer screening (LCS), but little is known about the perception of current smokers regarding LCS. We surveyed 122 current smokers between the ages of 55 and 80 years regarding their utilization and perceptions of LCS. Utilization of LCS was low, and few smokers were aware of LCS.

e123 Molecular Diagnostic Assays and Clinicopathologic Implications of *MET* Exon 14 Skipping Mutation in Non–small-cell Lung Cancer

Eun Kyung Kim, Kyung A. Kim, Chang Young Lee, Sangwoo Kim, Sunhee Chang, Byoung Chul Cho, Hyo Sup Shim

MET exon 14 skipping (*MET*ex14) has been reported as a biomarker that predicts the response to MET inhibitors. However, *MET*ex14 alterations exhibit a highly diverse sequence composition, posing a challenge for diagnostic testing in clinics. The present study showed that next-generation sequencing can be the first assay of choice as a multiplex testing and real-time quantitative reverse transcription polymerase chain reaction can be appropriate as a single gene testing. *MET*ex14 also had characteristic clinicopathologic features.