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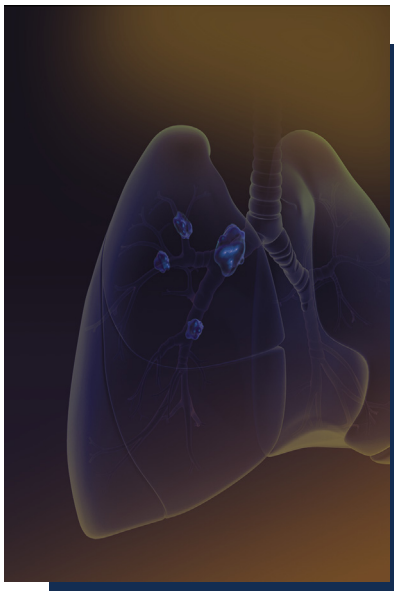

Illustration by Irin Moore

CLINICAL Lung Cancer

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Original Studies

258 Programmed Cell Death Ligand 1 Immunohistochemistry: A Concordance Study Between Surgical Specimen, Biopsy, and Tissue Microarray

Hedvig Elfving, Johanna Sofia Margareta Mattsson, Cecilia Lindskog, Max Backman, Uwe Menzel, Patrick Micke

Programmed cell death ligand 1 (PD-L1) expression within the same lung cancer tissue is variable. In this study we evaluated if the PD-L1 expression on small biopsy specimens represent the PD-L1 status of the corresponding resection specimen. Our results indicate a relative good agreement between biopsy and surgical specimens, with a discordance in approximately 10% of the cases.

263 Chemotherapy Versus Supportive Care for Unresected Malignant Pleural Mesothelioma

Vivek Verma, Rodney E. Wegner, Eric D. Brooks, Joseph A. Miccio, Benjamin H. Kann, Gene G. Finley, Moses S. Raj, Surbhi Grover, Pranshu Mohindra, Charles B. Simone, II

Management for unresected malignant pleural mesothelioma is largely limited to palliative chemotherapy and best supportive care. From this study, chemotherapy may benefit metastatic epithelioid and non-metastatic non-epithelioid malignant pleural mesothelioma to a greater degree than metastatic non-epithelioid disease.

270 Heterogeneous Expression of Programmed Death Receptor-ligand 1 on Circulating Tumor Cells in Patients With Lung Cancer

Yasuhiro Koh, Satomi Yagi, Hiroaki Akamatsu, Kuninobu Kanai, Atsushi Hayata, Nahomi Tokudome, Keiichiro Akamatsu, Masayuki Higuchi, Hisashige Kanbara, Masanori Nakanishi, Hiroki Ueda, Nobuyuki Yamamoto

Circulating tumor cells (CTCs) and their programmed death receptor-ligand 1 (PD-L1) expression in patients with lung cancer were detected using a microcavity array system. PD-L1 expression was detected in 73% of patients who harbored CTCs. The proportion of PD-L1-positive CTCs ranged from 3% to 100%, suggesting intra-patient heterogeneity. No correlation on PD-L1 expression was observed between tumor tissues and CTCs.

278 Efficacy and Safety of *BRAF* Inhibitors With or Without *MEK* Inhibitors in *BRAF*-Mutant Advanced Non–Small-Cell Lung Cancer: Findings From a Real-Life Cohort

Elizabeth Dudnik, Jair Bar, Nir Peled, Elias Bshara, Teodor Kuznetsov, Aharon Yonathan Cohen, Tzippy Shochat, Hovav Nechushtan, Amir Onn, Abed Agbarya, Mor Moskovitz, Shoshana Keren, Noa Popovits-Hadar, Damien Urban, Moshe Mishaeli, Natalie Maimon Rabinovich, Ronen Brenner, Alona Zer, Ofer Rotem, Laila C. Roisman, Mira Wollner, for the Israel Lung Cancer Group

Little is known regarding the performance of *BRAF* inhibitors (BRAFi) and BRAFi + *MEK* inhibitor (MEKi) combination in the real-life setting. A real-life cohort of *BRAF*-mutant (BRAFm) non–small-cell lung cancer (NSCLC) patients (n = 58) was analyzed, focusing on comparative efficacy and safety of BRAFi and BRAFi + MEKi combination. In V600E BRAFm NSCLC, BRAFi + MEKi are effective, well tolerated, and superior to BRAFi. Non–V600E kinase-active BRAFm NSCLC may respond to BRAFi + MEKi.

287 Real-World Clinical Impact of Immune Checkpoint Inhibitors in Patients With Advanced/Metastatic Non–Small Cell Lung Cancer After Platinum Chemotherapy

Lee Schwartzberg, Beata Korytowsky, John R. Penrod, Ying Zhang, T. Kim Le, Cory Batenchuk, Lee Krug

We compared real-world data from US patients who received second-line (2L) therapy for non–small-cell lung cancer before ("historical") and after ("current") US Food and Drug Administration approval of programmed death ligand 1 (PD-L1) inhibitors. A greater proportion of patients received 2L therapy in the current compared with the historical setting; approximately half of current patients received 2L PD-L1 inhibitors. Survival was improved by 15% in the current setting.

297 Relevance of Detection of Mechanisms of Resistance to ALK Inhibitors in ALK-Rearranged NSCLC in Routine Practice

Philippe Jamme, Clotilde Descarpentries, Radj Gervais, Eric Dansin, Marie Wislez, Valérie Grégoire, Nicolas Richard, Simon Baldacci, Nathalie Rabbe, Maeva Kyheng, Zoulika Kherrouche, Fabienne Escande, Marie Christine Copin, Alexis B. Cortot

Anaplastic lymphome kinase (*ALK*) mutations are responsible for resistance to ALK tyrosine kinase inhibitors (TKIs) in ALK-rearranged non—small-cell lung cancer but their frequency and relevance has not been assessed in routine practice. In this retrospective multicenter study, the *ALK* mutation rate was 15% and 33% after failure of treatment with 1 and 2 TKIs, respectively. Most of the patients harboring an *ALK* mutation achieved an objective response with subsequent ALK TKI treatment.

305 Indoor Radon in *EGFR*- and *BRAF*-Mutated and *ALK*-Rearranged Non—Small-Cell Lung Cancer Patients

Laura Mezquita, Amparo Benito, Alberto Ruano-Raviña, Javier Zamora, Maria Eugenia Olmedo, Pablo Reguera, Ainhoa Madariaga, María Villamayor, Silvia Patricia Cortez, Luis Gorospe, Almudena Santón, Sagrario Mayoralas, Raúl Hernanz, Alberto Cabañero, Edouard Auclin, Alfredo Carrato, Pilar Garrido

Radon is the first cause of lung cancer in nonsmokers according to the World Health Organization (WHO), which recommends not exceeding 100Bq/m^3 in homes. No risk factor has yet been identified for non—small-cell lung cancer (NSCLC) harboring driver alterations, mainly nonsmokers. We found a median concentration of 104 Bq/m^3, above the WHO recommendation in *EGFR*-mutated, *BRAF*-mutated, and *ALK*-rearranged NSCLC patients, with no differences between them.

313 Small-cell Lung Cancer in Very Elderly ($\geq$ 80 Years) Patients

Steven E. Schild, Liming Zhao, Jason A. Wampfler, Thomas B. Daniels, Terence Sio, Helen J. Ross, Harshita Paripati, Randolph S. Marks, Joanne Yi, Han Liu, Yanqi He, Ping Yang

This study found that the survival of very elderly ($\geq$ 80 years) patients with small-cell lung cancer was associated with stage, performance status, and treatment option. Very elderly patients with small-cell lung cancer are a growing patient population who have not been previously reported on. Future progress will require trials specific to the elderly, integration of immunotherapy, greater supportive care, better geriatric assessment, and less toxic regimens.

322 Predictors of Outcomes and a Scoring System for Estimating Survival in Patients Treated With Radiotherapy for Metastatic Spinal Cord Compression From Small-Cell Lung Cancer

Dirk Rades, Laura Motisi, Theo Veninga, Antonio Conde-Moreno, Jon Cacicedo, Steven E. Schild

This study identified significant predictors for improvement of motor deficits, ambulatory status, and overall survival after radiotherapy of metastatic spinal cord compression (MSCC) from small-cell lung cancer (SCLC). Furthermore, a survival score was developed including 3 groups with 6-month survival rates of 0, 18%, and 77%, respectively. The predictive factors and the survival score can support physicians aiming to prescribe personalized treatments to patients with MSCC from SCLC.

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

e421 Next-generation Sequencing for *ALK* and *ROS1* Rearrangement Detection in Patients With Non—small-cell Lung Cancer: Implications of FISH-positive Patterns

Sergi Clavé, Natalia Rodon, Lara Pijuan, Olga Díaz, Marta Lorenzo, Pedro Rocha, Álvaro Taus, Remei Blanco, Joaquim Bosch-Barrera, Noemí Reguart, Noelia de la Torre, Glòria Oliveras, Blanca Espinet, Beatriz Bellosillo, Xavier Puig, Edurne Arriola, Marta Salido

Detection of *ALK* and *ROS1* rearrangements was assessed using next-generation sequencing and immunohistochemistry in a retrospective cohort of 40 patients with non—small-cell lung cancer with known fluorescence in situ hybridization (FISH) data. Comparison between methods revealed that isolated 3′ signal FISH pattern might suggest a false-positive result. When used as a screening method, detailed reporting of FISH patterns should be strongly considered.

e430 Thoracic Oncology Multidisciplinary Clinic Reduces Unnecessary Health Care Expenditure Used in the Workup of Patients With Non—small-cell Lung Cancer

Khinh Ranh Voong, Ou Stella Liang, Patrick Dugan, Deirdre Torto, William V. Padula, James P. Senter, Margaret Lang, Craig M. Hooker, Josephine Feliciano, Stephen Broderick, Lonny Yarmus, Kanika Khanna, Amol Narang, Russell K. Hales

For patients with non—small-cell lung cancer requiring definitive multimodality care (radiation, chemotherapy, surgery), evaluation through a coordinated single-day multidisciplinary clinic reduced $5839 in hospital charges per patient during the 90-day diagnostic period prior to treatment when compared with evaluation through traditional sequential referral-based thoracic oncology clinics. This corresponded to a 23% charge reduction per patient.

e442 Pemetrexed in the Treatment of Leptomeningeal Metastasis in Patients With *EGFR*-mutant Lung Cancer

Mihong Choi, Bhumsuk Keam, Chan-Young Ock, Miso Kim, Tae Min Kim, Dong-Wan Kim, Dae Seog Heo

The role of pemetrexed in the treatment of leptomeningeal metastasis (LM) was examined retrospectively in 110 patients with *EGFR*-mutant lung cancer. Pemetrexed use after LM was independently associated with a survival benefit for patients with LM.

e452 Stereotactic Body Radiotherapy for Centrally Located Primary Non—Small-Cell Lung Cancer: A Meta-Analysis

Tosol Yu, In-Soo Shin, Won Sup Yoon, Chai Hong Rim

The feasibility of stereotactic body radiotherapy (SBRT) for centrally located tumors is controversial. SBRT with 100 Gy or higher biologically equivalent dose using an α/β of 10 Gy for centrally located primary NSCLC offered excellent local control (3years; 77.6% [95% confidential interval, 65.2-86.5]), comparable with that of other SBRT reports for peripheral lung tumors. The pooled rate of Grade $\geq$3 complications was 12.0%. This suggest that SBRT can be used in inoperable centrally located lung tumors with a curative intent.

e463 Node-Positive Segmentectomy for Non—Small-Cell Lung Cancer: Risk Factors and Outcomes

Waseem Lutfi, Matthew J. Schuchert, Rajeev Dhupar, Chigozirim Ekeke, Inderpal S. Sarkaria, Neil A. Christie, James D. Luketich, Olugbenga T. Okusanya

Segmentectomy for well-selected early stage non—small-cell lung carcinoma (NSCLC) has been shown to have similar survival compared to lobectomy. However, the outcomes of patients with node-positive disease is unknown. In this cohort of 4556 clinical stage I NSCLC patients with node-positive disease, segmentectomy was associated with similar overall survival compared to lobectomy.

e470 Relationship Between Prior Radiotherapy and Checkpoint-Inhibitor Pneumonitis in Patients With Advanced Non—Small-Cell Lung Cancer

Khinh Ranh Voong, Sarah Z. Hazell, Wei Fu, Chen Hu, Cheng Ting Lin, Kai Ding, Karthik Suresh, Jonathan Hayman, Russell K. Hales, Salem Alfaifi, Kristen A. Marrone, Benjamin Levy, Christine L. Hann, David S. Ettinger, Josephine L. Feliciano, Valerie Peterson, Ronan J. Kelly, Julie R. Brahmer, Patrick M. Forde, Jarushka Naidoo

In patients with non—small-cell lung cancer treated with anti—PD-1/PD-L1 agents, no specific radiation parameter was significantly associated with immune-related (IR) pneumonitis. We identify on subset analysis of patients who developed IR pneumonitis and received chest radiation, patients were numerically more likely to have received chest radiation with curative intent than with palliative intent (89% vs. 11%), that approached statistical significance.

e480 Impact of Corticosteroid Administration on Outcomes Following Stereotactic Ablative Radiotherapy for Non—small-cell Lung Cancer

Hongqi Li, Vivek Verma, Eric D. Brooks, Lei Feng, Tiening Zhang, James W. Welsh, Steven H. Lin, Daniel Gomez, Saumil Gandhi, John V. Heymach, Joe Y. Chang

Radiotherapy produces immune-promoting effects, which may be blunted by the delivery of corticosteroids. When analyzing 912 patients with T1-3N0M0 non—small-cell lung cancer treated with stereotactic ablative radiotherapy, corticosteroid administration (defined as within 2 days of the stereotactic ablative radiotherapy course) was not associated with an increased recurrence rate.

e489 Immune Checkpoint Inhibitor-Induced Myasthenia Gravis in a Patient with Advanced NSCLC and Remote History of Thymoma

Matthew S. Lara, Alaa Afify, Michael P. Ellis, Chinh T. Phan, David P. Richman, Jonathan W. Riess

e492 Phase I/II Study of Osimertinib With Bevacizumab in EGFR-mutated, T790M-positive Patients With Progressed EGFR-TKIs: West Japan Oncology Group 8715L (WJOG8715L)

Hiroaki Akamatsu, Shunsuke Teraoka, Satoshi Morita, Nobuyuki Katakami, Motoko Tachihara, Haruko Daga, Nobuyuki Yamamoto, Kazuhiko Nakagawa

e495 Chemotherapy and Radiation Versus Chemotherapy Alone for Elderly Patients With N3 Stage IIIB NSCLC

Angel Qin, Elizabeth Lusk, Stephanie Daignault-Newton, Bryan J. Schneider

We conducted a retrospective analysis in patients who received chemotherapy and radiation and chemotherapy alone for stage N3 IIIB non—small-cell lung cancer with a focus on those ≥70 years of age. We found that there was a survival benefit of bimodality therapy irrespective of age and comorbidities; they should not be routinely used to exclude patients from aggressive treatment.

e504 Clinical and Prognostic Significance of the Epithelial—Mesenchymal Transition in Stage IA Lung Adenocarcinoma: A Propensity Score—Matched Analysis

Taichi Matsubara, Tetsuzo Tagawa, Kazuki Takada, Gouji Toyokawa, Mototsugu Shimokawa, Yuka Kozuma, Takaki Akamine, Akira Haro, Atsushi Osoegawa, Masaki Mori

We aimed to analyze the clinical significance of the epithelial—mesenchymal transition (EMT) in stage IA lung adenocarcinoma. Tumors with the EMT phenotype were identified in 43.1% of patients with a high ratio of consolidation to tumor diameter. Propensity score matching indicated a significant association of the EMT with shorter survival.

e514 Characterization of Myeloid-derived Suppressor Cells in a Patient With Lung Adenocarcinoma Undergoing Durvalumab Treatment: A Case Report

Giacomo Bertelli, Rosalinda Trovato, Stefano Ugel, Emilio Bria, Michele Milella, Vincenzo Bronte, Sara Pilotto

e517 Concomitant *EGFR* Mutation and *EML4-ALK* Rearrangement in Lung Adenocarcinoma Is More Frequent in Multifocal Lesions

Jun Fan, Xiaofang Dai, Zhenkao Wang, Bo Huang, Heshui Shi, Danju Luo, Jiwei Zhang, Weijing Cai, Xiu Nie, Fred R. Hirsch

We retrospectively investigated the intertumoral heterogeneity of pathologic and genetic characteristics of multifocal lung adenocarcinomas (LUAC) with epidermal growth factor receptor (*EGFR*)/anaplastic lymphoma kinase (*ALK*) co-alterations. The prevalence of *EGFR/ALK* co-alterations was higher in the multifocal LUAC than in the unifocal LUAC. To determine appropriate treatment strategies, extensive molecular profiling could give us more information to distinguish primary lesions from metastatic lesions.

e531 Response to First-Line Osimertinib Treatment in Non—Small-Cell Lung Cancer With Coexisting G719A and Primary T790M Epidermal Growth Factor Receptor Mutations

Tomoo Ikari, Jun Sakakibara-Konishi, Gaku Yamamoto, Hidenori Kitai, Hidenori Mizugaki, Hajime Asahina, Eiki Kikuchi, Naofumi Shinagawa