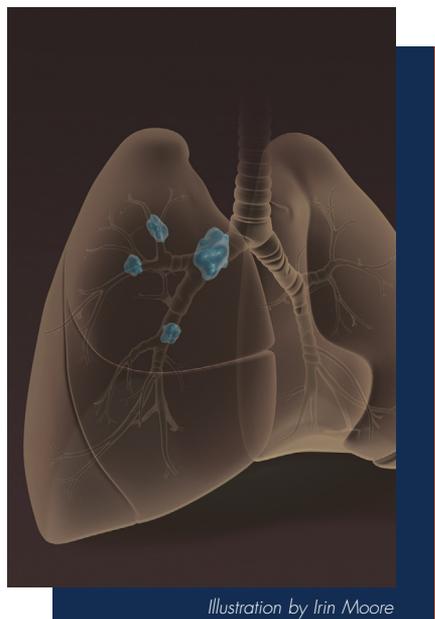


Table of Contents



CLINICAL Lung Cancer

November 2019 • Volume 20, Number 6

Original Studies

405 Clinical Characteristics, Molecular Phenotyping, and Management of Isolated Adrenal Metastases From Lung Cancer

Antonio Mazzella, Mauro Loi, Audrey Mansuet-Lupo, Antonio Bobbio, Helene Blons, Diane Damotte, Marco Alifano

Adrenal involvement is frequent in metastatic non–small-lung cancer. Patients with oligometastatic (≤ 3 metastases) disease treated with adrenalectomy have a 5-year overall survival of 34.5%. Next generation sequencing identified mutational discordance between primary tumors and metastases in 20% of cases, thus offering insights into tailored treatment in the setting of oligometastatic lung cancer.

412 Incorporation of the SUVmax Measured From FDG PET and Neutrophil-to-lymphocyte Ratio Improves Prediction of Clinical Outcomes in Patients With Locally Advanced Non–small-cell Lung Cancer

Dong Guo, Feng Jin, Wang Jing, Minghuan Li, Dawei Chen, Bing Zou, Guangdong Jiang, Lei Fu, Hui Zhu, Li Kong, Jing Wu, Jinming Yu, Jinbo Yue

Approximately 20% to 25% of patients with non–small-cell lung cancer (NSCLC) are diagnosed with locally advanced disease. Despite carefully implemented treatment, the survival outcomes of these patients remain poor, with 5-year overall survival rates of 10% to 20%, and locoregional recurrence rates of 35% to 70%. This retrospective analysis of 138 patients with locally advanced NSCLC was conducted to find out the prognostic factors and to improve prediction of clinical outcomes. Incorporation of the maximum standardized uptake value and neutrophil-to-lymphocyte ratio improves prediction of clinical outcomes in patients with locally advanced NSCLC.

420 Prognostic Significance of ^{18}F -FDG PET/CT Metabolic Parameters and Tumor Galectin-1 Expression in Patients With Surgically Resected Lung Adenocarcinoma

Hongna Zheng, Yan Cui, Xuena Li, Bulin Du, Yaming Li

Galectin-1 (Gal-1) is a regulatory checkpoint that promotes immunosuppression and cancer development. We examined Gal-1 expression through immunohistochemistry and found that there was a significant positive correlation between Gal-1 expression and positron emission tomography/computed tomography (PET/CT) metabolic parameters in patients with surgically resected lung adenocarcinoma. Our results highlight PET/CT can predict Gal-1 expression and prognosis in lung adenocarcinoma.

- 429 Increased Incidence of Lung Cancer Among Patients With Superficial Transitional Cell Carcinoma: A Potential Risk Cohort for Lung Cancer Screening**
Yaakov Tolwin, Roni Gillis, Inbar Nardi Agmon, Noa Shani Shrem, Eli Rosenbaum, Nir Peled
Current recommendations for lung cancer (LC) screening do not include transitional cell carcinoma of the bladder (TCC) as a risk factor for determining screening eligibility. On the basis of 91,606 patients with localized TCC, in this study we examined whether patients with bladder cancer have higher LC rates. We found that LC rates are indeed higher in these patients, and therefore, they might benefit from being screened for LC.
- 435 Dosimetric Predictors of Cardiotoxicity in Thoracic Radiotherapy for Lung Cancer**
Jenna F. Borkenhagen, Carmen Bergom, Cooper T. Rapp, Slade J. Klawikowski, Lisa E. Rein, Elizabeth M. Gore
When treating lung cancer with radiotherapy, higher cardiac doses are associated with worse overall survival, although the association with early cardiotoxicity is poorly understood. In this institutional retrospective review, the volume of ventricles receiving ≥ 45 Gy radiotherapy dose was associated with early cardiotoxicity. In practice, early cardiotoxicity is under-reported, supporting the need for detailed cardiac evaluations in high-risk patients.
- 442 Prognostic Impact and Risk Factors of Immune-Related Pneumonitis in Patients With Non–Small-Cell Lung Cancer Who Received Programmed Death 1 Inhibitors**
Jun Fukihara, Koji Sakamoto, Junji Koyama, Takayasu Ito, Shingo Iwano, Masahiro Morise, Masahiro Ogawa, Yasuhiro Kondoh, Tomoki Kimura, Naozumi Hashimoto, Yoshinori Hasegawa
Pneumonitis is one of the adverse events of programmed death 1 (PD-1) inhibitors. We retrospectively evaluated prognosis and risk factors of pneumonitis in patients with non–small-cell lung cancer taking a PD-1 inhibitor. The overall survival time was significantly shorter in patients with pneumonitis than in those without. Pembrolizumab (vs. nivolumab) use and low serum albumin were risk factors for pneumonitis.
- 451 Comparative Efficacy of Second- and Subsequent-line Treatments for Metastatic NSCLC: A Fractional Polynomials Network Meta-analysis of Cancer Immunotherapies**
Christian Schulz, David Gandara, Carmen G. Berardo, Rachel Rosenthal, Jason Foo, Chaienna Morel, Marcus Ballinger, Claire Watkins, Paula Chu
Cancer immunotherapies have advanced the second-line treatment of non–small-cell lung cancer. Evaluating the relative effect of these therapies requires methods accounting for the delayed clinical effect and longer-term survival rates that have been observed in anti-programmed death-ligand 1/programmed cell death protein 1 therapy trials. This study applied advanced statistical methods to compare clinical trial results across all second-line treatments. The immunotherapies offered superior efficacy in non–small-cell lung cancer.
- 461 Predictors of Respiratory Decline Following Stereotactic Ablative Radiotherapy to Multiple Lung Tumors**
Everett J. Moding, Rachel Liang, Frederick M. Lartey, Peter G. Maxim, Arthur Sung, Maximilian Diehn, Billy W. Loo, Jr, Michael F. Gensheimer
The safety and efficacy of stereotactic ablative radiation therapy to multiple lung tumors remains unclear. We retrospectively reviewed a total of 86 patients treated with stereotactic ablative radiation therapy to 203 lung tumors. We observed excellent local control and low rates of conventional metrics of toxicity, but there was a high rate of respiratory decline after treatment that warrants further study.
- 469 Subgroup Analysis of Japanese Patients in a Phase III Study of Atezolizumab in Extensive-stage Small-cell Lung Cancer (IMpower133)**
Makoto Nishio, Shunichi Sugawara, Shinji Atagi, Hiroaki Akamatsu, Hiroshi Sakai, Isamu Okamoto, Koichi Takayama, Hidetoshi Hayashi, Yuki Nakagawa, Tomohisa Kawakami
Atezolizumab is effective and well-tolerated in patients with extensive-stage small-cell lung cancer (ES-SCLC). We examined atezolizumab's efficacy and safety in 42 Japanese patients with ES-SCLC via a subanalysis of the phase I/III IMpower133 trial. Addition of atezolizumab to chemotherapy improved overall survival and was generally well-tolerated, thus offering a potentially new treatment for Japanese patients with ES-SCLC.

477 A Population-Based Study of Incidence and Survival of 1588 Thymic Malignancies: Results From the California Cancer Registry

David J. Benjamin, Amy Klapheke, Primo N. Lara, Rosemary D. Cress, Jonathan W. Riess

Because of limited population-based epidemiological studies on thymic malignancies in the current literature, we sought to evaluate incidence and survival trends in thymic malignancies in the California Cancer Registry. Among 1588 adult cases of thymic malignancy diagnosed between 1988 and 2015, we found that thymic malignancy incidence is rising and there is a variation in incidence according to race/ethnicity. As in previous studies, advanced stage and thymic carcinoma were found to be associated with worsened survival. There also appears to be a trend toward detecting more localized stage disease over time, possibly because of the increased use of thoracic imaging studies. Treatment with surgery was associated with improved overall survival in all stages of disease and improved cause-specific survival in local and regional disease. Further research is required to evaluate and better understand contemporary incidence and prognostic factors in thymic malignancies.

484 Survival Outcomes With Thoracic Radiotherapy in Extensive-Stage Small-Cell Lung Cancer: A Propensity Score-Matched Analysis of the National Cancer Database

Sibo Tian, Xinyan Zhang, Renjian Jiang, Rathi N. Pillai, Taofeek K. Owonikoko, Conor E. Steuer, Nabil F. Saba, Suchita Pakkala, Pretesh R. Patel, Chandra P. Belani, Fadlo R. Khuri, Walter J. Curran, Suresh S. Ramalingam, Madhusmita Behera, Kristin A. Higgins

The role of consolidative thoracic radiotherapy is unclear in extensive-stage small-cell lung carcinoma, for which chemotherapy is standard. We aimed to evaluate its effect on survival using a large national database using propensity-matching methods. On the basis of a cohort of >14,000 patients, we found its use in addition to chemotherapy was associated with a significant improvement in survival.

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

e593 ROS1-rearranged NSCLC With Secondary Resistance Mutation: Case Report and Current Perspectives

Florian Guisier, Nicolas Piton, Mathieu Salaun, Luc Thiberville

e597 Identifying Resistance Mechanisms to Osimertinib via Blood Biopsy

Michael J. Jelinek, Samantha A. Armstrong, Jyoti D. Patel, Deepa S. Subramaniam

e601 Prognostic Significance of Liver Metastasis in Durvalumab-Treated Lung Cancer Patients

Sriram Sridhar, Luis Paz-Ares, Hao Liu, Kui Shen, Chris Morehouse, Naiyer Rizvi, Neil H. Segal, Xiaoping Jin, Yanan Zheng, Rajesh Narwal, Ashok Gupta, Phillip A. Dennis, Jiabu Ye, Pralay Mukhopadhyay, Brandon W. Higgs, Koustubh Ranade

The prognostic value of baseline liver metastases (LMs) was evaluated in 569 patients with advanced/metastatic non-small-cell lung cancer receiving the programmed cell death ligand 1 (PD-L1) inhibitor durvalumab. LMs were an independent negative prognostic factor for survival and were associated with significantly lower objective response rates. However, PD-L1 as an independent factor predicted benefit from durvalumab.

e609 Clinical Outcomes of Up-front Surgery Versus Surgery After Induction Chemotherapy for Thymoma and Thymic Carcinoma: A Retrospective Study

Wei-Li Ma, Chia-Chi Lin, Feng-Ming Hsu, Jang-Ming Lee, Jin-Shing Chen, Min-Shu Hsieh, Yih-Leong Chang, Ying-Ting Chao, Chin-Hao Chang, James Chih-Hsin Yang

Results comparing the outcomes of up-front surgery and surgery after induction chemotherapy in thymic neoplasms are inconsistent. We assessed 204 patients undergoing up-front surgery, surgery after induction chemotherapy, and no surgery. Thymic carcinoma patients receiving up-front surgery had better overall survival. Multivariate analysis showed that thymic carcinoma pathology type and American Joint Committee on Cancer stage IVB are poor prognostic factors.

e619 Comment on the data of the article titled “Second Primary Non–Small-Cell Lung Cancer After Head and Neck Cancer: A Population-Based Study of Clinical and Pathologic Characteristics and Survival Outcomes in 3597 Patients”

Junmiao Wen

e620 Effectiveness of Treatments for Advanced Non–Small-Cell Lung Cancer With Exon 20 Insertion Epidermal Growth Factor Receptor Mutations

Jenn-Yu Wu, Chong-Jen Yu, Jin-Yuan Shih

There are no approved effective treatments in advanced non–small-cell lung cancer (NSCLC) patients with exon 20 insertion epidermal growth factor receptor (*EGFR*) mutations. In the present survey of 3805 NSCLC patients screened for *EGFR* mutations, 84 patients had an exon 20 insertion. Firstline pemetrexed-containing therapies were related to better outcomes. The mutation Ala763_Tyr764insPheGlnGluAla (A763_Y764 insFQEA) was related to a favorable response to tyrosine kinase inhibitors.

e631 Management of Central Nervous System Metastases in Patients With Advanced Anaplastic Lymphoma Kinase-Rearranged Non–Small-Cell Lung Cancer During Crizotinib Treatment

Yiming Zhao, Bo Zhang, Shuyuan Wang, Rong Qiao, Jianlin Xu, Lele Zhang, Yanwei Zhang, Baohui Han

The optimal treatment approach for central nervous system metastases in patients with anaplastic lymphoma kinase (*ALK*)-positive non–small-cell lung cancer on crizotinib has not been established. Those who receive a second *ALK* tyrosine kinase inhibitor (TKI), particularly brigatinib, showed superior clinical outcomes compared with other treatments. The newly approved TKIs showed promise in the control of brain metastases, even without radiotherapy.

e638 Assessment of a Radiomic Signature Developed in a General NSCLC Cohort for Predicting Overall Survival of *ALK*-Positive Patients With Different Treatment Types

Lyu Huang, Jiayan Chen, Weigang Hu, Xinyan Xu, Di Liu, Junmiao Wen, Jiayu Lu, Jianzhao Cao, Junhua Zhang, Yu Gu, Jiazhou Wang, Min Fan

Anaplastic lymphoma kinase (*ALK*)-positive (*ALK*⁺) patients exhibit unique clinical characteristics. It would be beneficial to effectively predict their treatment outcome. We assessed the performance of the radiomic signature from non–small-cell lung cancer for predicting *ALK*⁺ patient outcomes using the least absolute shrinkage and selection operator Cox regression model. Its performance was impaired when used for *ALK*⁺ patients treated with tyrosine kinase inhibitors (TKIs). Therefore, developing special signatures for patients treated with TKIs might be needed.

e652 The Prognostic Role of TNM Staging Compared With Tumor Volume and Number of Pleural Sites in Malignant Pleural Mesothelioma

Claudia Proto, Diego Signorelli, Sandra Mallone, Arsela Prelaj, Giuseppe Lo Russo, Martina Imbimbo, Giulia Galli, Roberto Ferrara, Monica Ganzinelli, Giovanni Leuzzi, Francesca Gabriella Greco, Giuseppina Calareso, Laura Botta, Gemma Gatta, Marina Garassino, Annalisa Trama

Malignant pleural mesothelioma (MPM) is an aggressive disease with a unique morphology and distribution. Because of its peculiar growth pattern, clinical staging is difficult. Quantitative assessment such as tumor volume (TV) was suggested as an alternative prognostic evaluation. In this study we aimed to compare the prognostic role of Tumor, Node, Metastases (TNM) clinical staging with that of alternative staging approaches on the basis of the use of 2 quantitative clinical parameters, TV and number of pleural sites (NPS), in MPM patients (pts). Our data confirmed the prognostic role of TNM, tumor size, TV, and NPS. However, the TV and NPS combination performed better than TV, NPS, and TNM alone as prognostic classifier. Considering different quantitative parameters and translating such an approach from research level to clinical practice could increase prognostic accuracy for MPM pts, and help clinicians choose the best therapeutic strategy.

e661 Spirituality and Emotional Distress Among Lung Cancer Survivors

Lisa M. Gudenkauf, Matthew M. Clark, Paul J. Novotny, Katherine M. Piderman, Shawna L. Ehlers, Christi A. Patten, Lise Solberg Nes, Kathryn J. Ruddy, Jeff A. Sloan, Ping Yang

The purpose of this study was to examine the relationship between spirituality and distress among lung cancer survivors. In a cohort of 864 lung cancer survivors, spirituality was associated with a lower prevalence of emotional distress, being married, fewer years of cigarette smoking, and better Eastern Cooperative Oncology Group performance status. Additionally, in patients who were experiencing low emotional distress at the time of diagnosis, spirituality was associated with a lower risk of experiencing high emotional distress at a 1-year follow-up.

e667 Long-term Follow-up and Patterns of Recurrence of Patients With Oligometastatic NSCLC Treated With Pulmonary SBRT

Juliane Hörner-Rieber, Denise Bernhardt, Oliver Blanck, Marciana Duma, Hans Th. Eich, Sabine Gerum, Eleni Gkika, Peter Hass, Christoph Henkenberens, Hans-Ulrich Herold, Guido Hildebrandt, Detlef Imhoff, Henning Kahl, Stefan Janssen, Katrin Jurianz, Robert Krempien, Stefan Friedrich Lautenschläger, Fabian Lohaus, Arndt-Christian Mueller, Cordula Petersen, Irina Sackerer, Davide Scafa, Elsga Schrade, Lorenz Uhlmann, Andrea Wittig, Matthias Guckenberger

This multicenter analysis included 301 patients with oligometastatic non–small-cell lung cancer treated with pulmonary stereotactic body radiotherapy for 336 lung metastases. In routine clinical practice, stereotactic body radiotherapy for pulmonary oligometastatic non–small-cell lung cancer achieved favorable local control and promising overall survival. The dominant failure pattern was distant with a continuously high risk of disease progression for many years. Prospective studies should therefore combine local therapy with novel systemic treatments.