

Table of Contents



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CLINICAL Lung Cancer

May 2019 • Volume 20, Number 3

Perspective

- 143 Perspectives: Neutrophil-to-lymphocyte Ratio as a Potential Biomarker in Immune Checkpoint Inhibitor for Non–Small-Cell Lung Cancer

Wungki Park, Gilberto Lopes

Review

- 148 Advancements in Small-cell Lung Cancer: The Changing Landscape Following IMpower-133

Jose Pacheco, Paul A. Bunn

Original Studies

- 161 *EGFR* Gene Polymorphism Predicts Improved Outcome in Patients With *EGFR* Mutation-positive Non–small cell Lung Cancer Treated With Erlotinib

Anne Winther-Larsen, Eva Boysen Fynboe Ebert, Peter Meldgaard, Boe Sandahl Sorensen

A polymorphism in the *epidermal growth factor receptor (EGFR)* gene (181946C>T) was evaluated as a predictor of outcome in 75 patients with *EGFR* mutation-positive, non–small cell lung cancer treated with an *EGFR*-targeting tyrosine kinase inhibitor. Significantly longer progression-free survival and overall survival was found in patients harboring the 181946CT genotype. The polymorphism could be an important predictor of treatment response.

- 167 Cancer Stem Cell Biomarkers in *EGFR*-Mutation–Positive Non–Small-Cell Lung Cancer

Jordi Codony-Servat, Carles Codony-Servat, Andrés Felipe Cardona, Ana Giménez-Capitán, Ana Drozdowskyj, Jordi Berenguer, Jillian Wilhelmina Paulina Bracht, Masaaki Ito, Niki Karachaliou, Rafael Rosell

Epidermal growth factor receptor (*EGFR*) signaling deregulation promotes cancer stem cell (CSC) enrichment in non–small-cell lung cancer (NSCLC). In vitro experiments showed that inhibition of *EGFR*, signal transducer and activator of transcription 3 (*STAT3*), and *Src* decreased the CSC subpopulation. High expression of aldehyde dehydrogenase (*ALDH*) 1 isoforms and target hairy and enhancer of split 1 (*HES1*) was predictive of worse outcome to *EGFR* inhibition in *EGFR*-mutation–positive NSCLC patients. *ALDH1*, *HES1*, and B-cell–specific Moloney murine leukemia virus integration site 1 (*Bmi-1*) could be useful as biomarkers to monitor clinical progression, and the use of *STAT3* and *Src* inhibitors could be useful to inhibit the CSC subpopulation induced by *EGFR* inhibitor treatment.

- 178 Safety and Efficacy of Nivolumab in Patients With Advanced Non–small-cell Lung Cancer Treated Beyond Progression**
Biagio Ricciuti, Carlo Genova, Maria Bassanelli, Andrea De Giglio, Marta Brambilla, Giulio Metro, Sara Baglivo, Maria Giovanna Dal Bello, Anna Ceribelli, Francesco Grossi, Rita Chiari
- The possibility of delayed immune-related responses implies that patients who experience progressive disease may benefit from treatment with immunotherapy beyond progression (TBP). Here we demonstrated that a substantial proportion of patients with non–small-cell lung cancer treated with nivolumab, who were clinically stable and judged to be eligible for TBP derive a significant survival benefit from TBP. TBP is feasible and safe, and reduction or stabilization of target lesions may occur when patients with non–small-cell lung cancer continue nivolumab after initial progression. Discontinuation of nivolumab based only on radiologic progression might be premature.
- 186 Predictors of Nodal and Metastatic Failure in Early Stage Non–small-cell Lung Cancer After Stereotactic Body Radiation Therapy**
Alberto Cerra-Franco, Sheng Liu, Michella Azar, Kevin Shiue, Samantha Freije, Jason Hinton, Christopher R. Deig, Donna Edwards, Neil C. Estabrook, III, Susannah G. Ellsworth, Ke Huang, Khalil Diab, Mark P. Langer, Richard Zellars, Feng-Ming Kong, Jun Wan, Tim Lautenschlaeger
- Many patients with early stage non–small-cell lung cancer develop metastases after stereotactic body radiation therapy. We retrospectively analyzed multiple variables in 406 lesions to develop a predictor for metastatic failure. Gross tumor volume and prescription dose were significantly associated with metastases. A metastasis risk score tool was developed to identify patients at higher risk for metastases after lung stereotactic body radiation therapy who might benefit from enrollment in future trials evaluating the benefit of adjuvant or intensified treatment.
- 194 Disparities in the Treatment and Outcome of Stage I Non–Small-Cell Lung Cancer in the 21st Century**
Shraddha M. Dalwadi, Gary D. Lewis, Eric H. Bernicker, E. Brian Butler, Bin S. Teh, Andrew M. Farach
- Racial disparities are historically profound and affect outcomes in early stage non–small-cell lung cancer. We aimed to explore if recent advances in radiotherapy and surgery have improved epidemiological differences in outcomes related to race. African American patients continued to do worse in a contemporary Surveillance, Epidemiology, and End Results data set, because of increased association with T2 disease, older age, squamous histology, male sex, and suboptimal treatment.
- 201 Association Between Immune-related Adverse Events and Efficacy of Immune Checkpoint Inhibitors in Non–small-cell Lung Cancer**
Mathieu Grangeon, Pascale Tomasini, Solene Chaleat, Arnaud Jeanson, Maxime Souquet-Bressand, Nataliya Khobta, Julien Bermudez, Youssef Trigui, Laurent Greillier, Marilyne Blanchon, Mohamed Boucekine, Celine Mascaux, Fabrice Barlesi
- Immune checkpoints inhibitors (ICIs) in advanced non–small-cell lung cancer are associated with immune-related adverse events (IRAEs). We retrospectively analyzed the efficacy of ICIs in a cohort of 270 patients with the objective to assess the association of IRAEs with ICI efficacy. We found a statistically significant efficacy difference in favor of patients with IRAEs. These results could be used to determine ICI responders.
- 208 Activity of Nivolumab and Utility of Neutrophil-to-Lymphocyte Ratio as a Predictive Biomarker for Advanced Non–Small-Cell Lung Cancer: A Prospective Observational Study**
Tomoya Fukui, Yuriko Okuma, Yoshiro Nakahara, Sakiko Otani, Satoshi Igawa, Masato Katagiri, Hisashi Mitsufuji, Masaru Kubota, Yasuhiro Hiyoshi, Mikiko Ishihara, Masashi Kasajima, Jiichiro Sasaki, Katsuhiko Naoki
- Immune checkpoint inhibitor has greatly altered the standard of care for patients with advanced non–small-cell lung cancer (NSCLC). This prospective study reported the benefits of nivolumab in a routine clinical practice. Furthermore, neutrophil-to-lymphocyte ratio was identified as a candidate of predictive markers in nivolumab-treated NSCLC patients.

215 Efficacy and Safety of Lorlatinib in Korean Non–Small-Cell Lung Cancer Patients With *ALK* or *ROS1* Rearrangement Whose Disease Failed to Respond to a Previous Tyrosine Kinase Inhibitor
Jiyun Lee, Jong-Mu Sun, Se-Hoon Lee, Jin Seok Ahn, Keunchil Park, Yoon La Choi, Myung-Ju Ahn
The efficacy of lorlatinib, a novel third-generation tyrosine kinase inhibitor (TKI), has not been widely validated in Asian non–small-cell lung cancer (NSCLC) patients. We found an overall response rate of 64% and a disease control rate of 91% for Asian NSCLC patients harboring *ALK/ROS1* mutations. Lorlatinib is an important novel strategy for Asian NSCLC patients with disease progression after treatment with first- and second-generation TKIs.

222 Clinical Relevance of *EGFR*- or *KRAS*-mutated Subclones in Patients With Advanced Non–small-cell Lung Cancer Receiving Erlotinib in a French Prospective Cohort (IFCT ERMETIC2 Cohort - Part 2)
Michèle Beau-Faller, Matthieu Texier, Hélène Blons, Nicolas Richard, Fabienne Escande, Samia Melaabi, Sarab Lizard, Florence De Fraipont, Elisabeth Longchamp, Franck Morin, Gérard Zalcman, Jean-Pierre Pignon, Jacques Cadranet
Detecting driver mutations belongs now to the best practices in advanced/metastatic non–small-cell lung cancer. New molecular techniques are highly sensitive. In non–small-cell lung cancer treated with erlotinib (n = 228), we report that *EGFR*- and *KRAS*-mutated subclones had a prognostic value, but not minor *KRAS*-mutated subclones. Molecular techniques must be sensitive but not under 1% of mutated tumor cells.

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e219 Clinical Benefit From BRAF/MEK Inhibition in a Double Non-V600E BRAF Mutant Lung Adenocarcinoma: A Case Report
Roxana Reyes, Clara Mayo-de-las-Casas, Cristina Teixidó, Carlos Cabrera, Elba Marín, Ivan Vollmer, Pedro Jares, Mónica Garzón, Miguel Ángel Molina-Vila, Noemí Reguart

e224 A Patient With Lung Adenocarcinoma With *BRAF* Gene Fusion and Response to Vemurafenib
You-cai Zhu, Wen-xian Wang, Chun-wei Xu, Wu Zhuang, Kai-qi Du, Gang Chen, Tang-feng Lv, Yong Song

e229 Case Report: Temporal Heterogeneity of *ALK* Activating Mutations in Sequential *ALK* TKI–Treated Non–Small-Cell Lung Cancer Revealed Using NGS-Based Liquid Biopsy
Meijuan Ding, Lili Deng, Ruoying Yu, Dan Lu, Yun Bai, Xue Wu, Yang W. Shao, Yu Yang

e233 Durable Clinical Response to Crizotinib in *IRF2BP2-NTRK1* Non–small-cell Lung Cancer
Buhai Wang, Ye Gao, Yuxiang Huang, Qiuxiang Ou, Tingting Fang, Chunhui Tang, Xue Wu, Yang W. Shao

e238 EBV-positive Primary Pulmonary Lymphoepithelioma-like Carcinoma Response to PD-L1 Blockade
Anand Narayanan, Friedrich D. Knollmann, Julie Ann S. Walby, Steffany Lim, David R. Gandara, Jonathan W. Riess

e242 Immune Checkpoint Blockade Is Associated With Durable Responses in Pulmonary Sarcomatoid Carcinoma
Vineeth Sukrihan, Jason Sandler, Rasim Gucalp, Richard Gralla, Balázs Halmos

e247 Immunosuppression for Immune Checkpoint-related Toxicity Can Cause *Pneumocystis Jirovecii* Pneumonia (PJP) in Non–small-cell Lung Cancer (NSCLC): A Report of 2 Cases
Michael Schwarz, Florian Kocher, Dora Niedersuess-Beke, Jakob Rudzki, Maximilian Hochmair, Gerlig Widmann, Wolfgang Hilbe, Andreas Pircher

e251 Combined Use of Crizotinib and Gefitinib in Advanced Lung Adenocarcinoma With Leptomeningeal Metastases Harboring *MET* Amplification After the Development of Gefitinib Resistance: A Case Report and Literature Review
Yalun Li, Rui Zhang, Yongzhao Zhou, Juan Song, Wenxin Luo, Panwen Tian, Weimin Li

- e256 Impact of EGFR Mutation and ALK Translocation on Recurrence Pattern After Definitive Chemoradiotherapy for Inoperable Stage III Non-squamous Non-small-cell Lung Cancer**
Masaki Nakamura, Shun-ichiro Kageyama, Seiji Niho, Masayuki Okumura, Hidehiro Hojo, Atsushi Motegi, Naoki Nakamura, Sadamoto Zenda, Kiyotaka Yoh, Koichi Goto, Tetsuo Akimoto
We evaluated the failure pattern after definitive chemoradiotherapy in patients with stage III non-small-cell lung cancer harboring epidermal growth factor receptor mutations and/or anaplastic lymphoma kinase translocation. Although the epidermal growth factor receptor-mutant group showed a lower incidence of in-field failure and higher incidence of out-of-field failure, the group with anaplastic lymphoma kinase translocation showed no characteristic in-field or out-of-field failure pattern.
- e265 A Prospective, Randomized Trial for the Comparison of 19-G and 22-G Endobronchial Ultrasound-Guided Transbronchial Aspiration Needles; Introducing a Novel End Point of Sample Weight Corrected for Blood Content**
Celina Wolters, Kaid Darwiche, Daniel Franzen, Thomas Hager, Beata Bode-Lesnievska, Peter J. Kneuert, Kai He, Michael Koenig, Lutz Freitag, Lai Wei, Stephan Eisenmann, Christian Taube, Gerhard Weinreich, Filiz Oezkan
The demand for tissue has increased in lung cancer through personalized medicine. Recently, larger endobronchial ultrasound needles have become available for transbronchial lymph node biopsy. We compared the new 19-gauge (G) needle with 22-G needles regarding tissue quality, feasibility, safety, and performance in a prospective manner. Significantly more tissue and tumor cells per slide were obtained with a 19-G needle.
- e274 Intracranial Responses to Afatinib at Different Doses in Patients With EGFR-mutated Non-small-cell Lung Carcinoma and Brain Metastases**
Yu-Feng Wei, Chor-Kuan Lim, Mao-Song Tsai, Ming-Shyan Huang, Kuan-Yu Chen
Afatinib is commonly used for advanced EGFR-mutated non-small-cell lung cancer, and dose reduction is frequently required. The effect of dose reduction on brain metastasis was seldom investigated. This retrospective multicenter study analyzed different daily doses of afatinib used in treatment-naive patients with EGFR-mutated non-small-cell lung cancer and brain metastases, which demonstrated that dose reduction may not affect intracranial responses to afatinib therapy.
- e284 Inoperable Pulmonary Carcinoid Tumors: Local Control Rates With Stereotactic Body Radiotherapy/Hypofractionated RT With Image-Guided Radiotherapy**
Deepinder Singh, Yuhchyan Chen, Michael A. Cummings, Michael T. Milano
Pulmonary carcinoid tumors are rare and generally treated surgically. Hypofractionated radiotherapy, delivered in a precise manner via stereotactic body radiotherapy (SBRT), is a good alternative for patients not amenable to surgery. We treated 10 patients with 12 lesions using 5- to 10-fraction SBRT/hypofractionated regimens with excellent local control rates. SBRT appears to offer a promising approach for patients with inoperable pulmonary carcinoid tumors, which needs further investigation.
- e291 Palliative Care Referrals for Advanced Non-small-cell Lung Cancer (NSCLC): Patient and Provider Attitudes and Practices**
Emily Feld, Eric K. Singhi, Sharon Phillips, Li-Ching Huang, Yu Shyr, Leora Horn
Early palliative care implementation has been shown to be beneficial for patients with metastatic non-small-cell lung cancer. This study surveyed United States oncologists and patients with metastatic non-small-cell lung cancer on their practices and attitudes regarding the role of early palliative care referral. Our study highlights that few patients are referred at the time of diagnosis, likely owing to several noteworthy barriers.
- e299 Ex Vivo Interferon Gamma Production by Peripheral Immune Cells Predicts Survival in Lung Adenocarcinoma**
Sung Soo Ahn, Minkyung Kwon, Mindong Sung, Seung Min Jung, Sang-Won Lee, Yong-Beom Park, Sang Taek Kim, Jason Jungsik Song
Immunotherapies targeting the immune checkpoint receptor have shown promising results in non-small-cell lung cancer. Nevertheless, there are limitations in current biomarkers for evaluating the function of immune cells. Interferon gamma (IFN- γ) is a proinflammatory cytokine that contributes to cancer recognition and elimination. This study demonstrated ex vivo IFN- γ production might be a biomarker for predicting patient prognosis in lung adenocarcinoma.

e309 Transthoracic Rebiopsy for Mutation Analysis in Lung Adenocarcinoma: Outcomes and Risk Factors for the Acquisition of Nondiagnostic Specimens in 199 Patients

Bo Da Nam, Tae Jung Kim, Keunchil Park, Myung-Ju Ahn, Yoon-La Choi, Myung Jin Chung, Tae Sung Kim, Kyung Soo Lee

We investigated the clinical and procedure-related risk factors for the acquisition of nondiagnostic transthoracic rebiopsy specimens. The adequacy rate for tissue samples for mutation analysis was 90%. An internal low-attenuation area in the target lesion on computed tomography was an independent predictor for the acquisition of nondiagnostic specimens for mutation analysis during rebiopsy.

e317 Phase 1 Study of Cabozantinib in Japanese Patients With Expansion Cohorts in Non–Small-Cell Lung Cancer

Hiroshi Nokihara, Makoto Nishio, Noboru Yamamoto, Yutaka Fujiwara, Hidehito Horinouchi, Shintaro Kanda, Atsushi Horiike, Fumiyoshi Ohyanagi, Noriko Yanagitani, Linh Nguyen, Yifan Yaron, Anne Borgman, Tomohide Tamura

Cabozantinib was evaluated in 43 Japanese patients with advanced solid tumors. The maximum tolerated dose of cabozantinib capsules was determined to be 60 mg daily, and the recommended phase 2 dose of cabozantinib tablets was determined to be 60 mg daily. Cabozantinib had a manageable safety profile and antitumor activity in non–small-cell lung cancer.

e329 Clinical Features and Prognosis of Pulmonary Lymphoepithelioma-like Carcinoma: Summary of Eighty-five Cases

Yinyin Qin, Guoying Gao, Xiaohong Xie, Zheng Zhu, Weijie Guan, Xinqing Lin, Zhanhong Xie, Ouyang Ming, Rongchang Chen, Nanshan Zhong, Shiyue Li, Chengzhi Zhou

Pulmonary lymphoepithelioma-like carcinoma (PLELC) is a rare subtype of lung cancer. This retrospective analysis of 85 patients with PLELC was conducted to find the prognostic factors and to explore better treatment. PLELC had a better prognosis. Surgery was recommended mainly for the early stage and multimodality treatment for the advanced stage.

e338 Effect of Coexisting *KRAS* and *TP53* Mutations in Patients Treated With Chemotherapy for Non–small-cell Lung Cancer

Pascale Tomasini, Celine Mascaux, Kevin Jao, Catherine Labbe, Suzanne Kamel-Reid, Tracy Stockley, David M. Hwang, Natasha B. Leighl, Geoffrey Liu, Penelope A. Bradbury, Melania Pintilie, Ming-Sound Tsao, Frances A. Shepherd

The LACE-Bio group found adjuvant chemotherapy to be deleterious in non–small-cell lung cancer with coexisting *KRAS/TP53* mutations. We analyzed 218 patients with non–small-cell lung cancer (28 with coexisting *KRAS/TP53* mutations, 77 with *TP53* mutations, 37 with *KRAS* mutations, and 76 with no *KRAS/TP53* mutations) who received chemotherapy. There was no difference in disease-free or progression-free survival between the 4 groups. Overall survival was longer in the no *KRAS/TP53* group.

e346 Role of Skip Mediastinal Lymph Node Metastasis for Patients With Resectable Non–small-cell Lung Cancer: A Propensity Score Matching Analysis

Lin Wang, Cheng Zhan, Jie Gu, Junjie Xi, Zongwu Lin, Liang Xue, Di Ge, Qun Wang

Stage N2 non–small-cell lung cancer shows prognostic heterogeneity. We investigated the prognostic relevance of skip N2 in patients with N2 non–small-cell lung cancer using propensity score matching. Skip N2 was significantly associated with the better survival outcomes in patients with a tumor size ≤ 3 cm or with single N2 station involvement. Subgroups of patients with stage N2 disease may improve the accuracy of prognostic prediction.

e356 Increased Galectin-1 Expression in Thymic Epithelial Tumors

Jonathan W. Riess, Christina S. Kong, Robert B. West, Sukhmani K. Padda, Joel W. Neal, Heather A. Wakelee, Quynh-Thu Le

Thymic malignancies are rare tumors where lack of preclinical models adversely affect development of new therapies. Galectin-1 is an important protein in cancer involved in maintaining an immunosuppressive environment. This study examined galectin-1 expression in a large thymic epithelial tumor issue microarray and found elevated expression compared to benign thymus controls. Galectin-1 is a potential therapeutic target in thymic malignancies.

- e362 Phase 1b/2 Randomized Study of MEDI-575 in Combination With Carboplatin Plus Paclitaxel Versus Carboplatin Plus Paclitaxel Alone in Adult Patients With Previously Untreated Advanced Non–Small-Cell Lung Cancer**
Paul Wheatley-Price, Shirish Gadgeel, Toshiaki Takahashi, Xia Li, Mohammed Dar, George R. Blumenschein, Jr
Platelet-derived growth factor receptor blockade was explored as a potential mechanism to improve the efficacy of firstline therapy in patients with advanced non–small-cell lung cancer (NSCLC). In this phase 1b/2 study, therapy with MEDI-575, carboplatin, and paclitaxel (n = 53) did not improve progression-free survival versus carboplatin and paclitaxel alone (n = 46), and resulted in a higher rate of adverse events in patients with treatment-naive advanced NSCLC.
- e369 Prognostic Understanding and Quality of Life in Patients With Advanced Lung Cancer: A Multicenter Study**
Annelies Janssens, Sofia Derijcke, Daniëlle Galdermans, Marc Daenen, Veerle Surmont, Els De Droogh, Anneke Lefebure, Erika Saenen, Elke Vandenbroucke, Ann-Marie Morel, Anna Sadowska, Jan P. van Meerbeeck
Communication about the palliative setting remains difficult for many physicians. This seems a valid concern. Our study has shown that prognostic understanding will be associated with poorer emotional well-being and more pain but not with a worse mood. A poor mood has a detrimental effect on all aspects of quality of life. Our data suggest the need for psychological support, in addition to communication about the palliative setting.
- e376 Peptide Receptor Radionuclide Therapy for Patients With Advanced Lung Carcinoids**
Boris G. Naraev, Robert A. Ramirez, A. Tuba Kendi, Thorvardur R. Halfdanarson
- e393 Immunotherapy for LELC: Case Report and a Focused Review**
Marie Darrason, Antoine Martin, Michael Soussan, Kader Chouahnia, Marie-Christine Paillet, Hanene Boudabous, Pierre-Yves Brillet, Guilhem Bousquet, Laurent Zelek, Boris Duchemann
- e402 Rationale and Design of a Phase II Trial of Osimertinib Combined With Bevacizumab in Patients With Untreated Epidermal Growth Factor Receptor-mutated Non–small-cell Lung Cancer and Malignant Pleural and/or Pericardial Effusion (SPIRAL II Study)**
Osamu Hiranuma, Junji Uchino, Tadaaki Yamada, Yusuke Chihara, Nobuyo Tamiya, Yoshiko Kaneko, Kenichi Yoshimura, Koichi Takayama
- e407 Afatinib With Pembrolizumab for Treatment of Patients With Locally Advanced/Metastatic Squamous Cell Carcinoma of the Lung: The LUX-Lung IO/KEYNOTE 497 Study Protocol**
Benjamin Levy, Luis Paz-Ares, Jaafar Bennouna, Enriqueta Felip, Delvys Rodríguez Abreu, Dolores Isla, Fabrice Barlesi, Olivier Molinier, Jeannick Madelaine, Clarisse Audigier-Valette, Sang-We Kim, Hye Ryun Kim, Mustafa Ozguroglu, Mustafa Erman, Firas Benyamine Badin, Tarek M. Mekhail, Ronald Scheff, Michael J. Chisamore, Behbood Sadrolhefazi, Jonathan W. Riess
- e413 Exploiting Fasting-mimicking Diet and METformin to Improve the Efficacy of Platinum-pemetrexed Chemotherapy in Advanced LKB1-inactivated Lung Adenocarcinoma: The FAME Trial**
Claudio Vernieri, Diego Signorelli, Giulia Galli, Monica Ganzinelli, Massimo Moro, Alessandra Fabbri, Elena Tamborini, Mirko Marabese, Elisa Caiola, Massimo Broggin, Lital Hollander, Rosaria Gallucci, Giulia Vandoni, Cecilia Gavazzi, Tiziana Triulzi, Mario Paolo Colombo, Angela Maria Rizzo, Paola Antonia Corsetto, Giancarlo Pruneri, Filippo de Braud, Gabriella Sozzi, Valter Torri, Marina Chiara Garassino
- e418 MET Immunohistochemistry Should Be Avoided in Selecting Non–small-cell Lung Cancers Requiring MET Exon 14 Skipping Mutation Analysis**
Laetitia Lambros, Arnaud Uguen