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Perspective

321 Algorithm for Codevelopment of New Drug-Predictive Biomarker Combinations: Accounting for Inter- and Intrapatient Tumor Heterogeneity

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Original Studies

340 Pemetrexed Therapy in Elderly Patients With Good Performance Status: Analysis of Two Phase III Trials of Patients With Nonsquamous Non–Small-Cell Lung Cancer

Cesare Gridelli, Thomas Brodowicz, Corey J. Langer, Patrick Peterson, Mominul Islam, Susan C. Guba, Patti Moore, Carla M. Visseren-Grul, Giorgio Scagliotti

The efficacy and safety of pemetrexed treatment was evaluated in elderly patients with nonsquamous advanced non-small-cell lung cancer and a performance status of 0-1. Data from 2 large randomized studies were retrospectively analyzed for patients aged <65 years, \geq 65 years and < 70 years, \geq 70 years. Safety and efficacy were similar between older and younger groups. Pemetrexed (first-line treatment combined with cisplatin or as maintenance therapy) is a viable treatment option for these patients.

347 Phase I and II Trials of Vinorelbine With Carboplatin for Patients 75 Years of Age or Older With Previously Untreated Non–Small-Cell Lung Cancer

Hiroshi Takatani, Yoichi Nakamura, Seiji Nagashima, Hiroshi Soda, Akitoshi Kinoshita, Minoru Fukuda, Masaaki Fukuda, Yoshifumi Soejima, Takashi Kasai, Katsumi Nakatomi, Tetsuya lida, Mikio Oka, Kazuhiro Tsukamoto, Shigeru Kohno

We conducted clinical trials to evaluate the safety and efficacy of vinorelbine and carboplatin for patients aged \geq 75 years and with advanced non-small-cell lung cancer. The use of 20 mg/m² vinorelbine on days 1 and 8 followed by carboplatin with an area under the curve of 4 mg/mL/min on day 1 every 4 weeks was warranted for such patients.

352 Proton Therapy With Concurrent Chemotherapy for Non–Small-Cell Lung Cancer: Technique and Early Results Bradford S. Hoppe, Stella Flampouri, Randal H. Henderson, Dat Pham, Abubakr A. Bajwa,

Harry D'Agostino, Soon N. Huh, Zuofeng Li, Nancy P. Mendenhall, R. Charles Nichols Little clinical data are available regarding toxicity from high-dose proton therapy with chemotherapy in stage III non-small-cell lung

cancer. The present study evaluates the early experience with this treatment regimen at the University of Florida Proton Therapy Institute in patients with regionally advanced non-small-cell lung cancer. Toxicity and local control rates were encouraging, and further investigation with proton therapy is warranted in these patients.

359 Multimodality Treatment and Long-Term Follow–Up of the Primary Pulmonary Lymphoepithelioma-Like Carcinoma Chung-Jen Huang, An-Chen Feng, Yueh-Fu Fang, Wen-Hui Ku, Nei-Min Chu, Chih-Teng Yu, Chia-Chuan Liu, Ming-Yuan Lee, Li-Han Hsu, Stella Y.C. Tsai, Chih-Shiun Shih, Chih-Liang Wang

Primary pulmonary lymphoepithelioma-like carcinoma is a very rare subtype of non-small-cell lung cancer. This retrospective study enrolled 21 patients and aimed to evaluate the long-term response under multimodality treatment. Primary pulmonary lymphoepithelioma-like carcinoma had a better prognosis compared with other non-small-cell lung cancers. Accurate pathologic diagnosis is recommended before cancer treatment.

363 Delay Between the Initial Symptoms, the Diagnosis and the Onset of Specific Treatment in Elderly Patients With Lung Cancer

Etienne Giroux Leprieur, Sylvie Labrune, Violaine Giraud, Thierry Gendry, Daniel Cobarzan, Thierry Chinet

No specific data are available concerning diagnostic and treatment delays and initial symptoms for elderly patients with lung cancer. We reviewed 193 patients (92 patients \geq 70 years old) with lung cancer. Unexpectedly, despite more comorbidities in the elderly patients, no difference was observed concerning diagnostic and treatment delays compared with younger patients, and the initial symptoms were equivalent.

369 Direct Comparison of 3 PCR Methods in Detecting EGFR Mutations in Patients with Advanced Non–Small-Cell Lung Cancer

Takaya Ikeda, Yoichi Nakamura, Hiroyuki Yamaguchi, Nanae Tomonaga, Seiji Doi, Katsumi Nakatomi, Tetsuya lida, Kohei Motoshima, Kosuke Mizoguchi, Takeshi Nagayasu, Kazuhiro Tsukamoto, Shigeru Kohno

We compared 3 polymerase chain reaction (PCR) methods (mutant-enriched PCR, peptide nucleic acid-locked nucleic acid [PNA-LNA] PCR, and PCR clamp) to detect *EGFR* mutations in 50 patients with advanced non-small-cell lung cancer (NSCLC). Seventeen were harboring *EGFR* mutations, 5 of whom showed discrepancies between the results of different PCR methods. All 5 responded to gefitinib, which we consider to suggest that the discrepancies were false negatives.

375 Association of Nuclear YB-1 Localization With Lung Resistance-related Protein and Epidermal Growth Factor Receptor Expression in Lung Cancer

Akira Hyogotani, Ken-ichi Ito, Kazuo Yoshida, Hiroto Izumi, Kimitoshi Kohno, Jun Amano

Nuclear Y-box binding protein 1 (YB-1) expression significantly correlated with positive lung resistance-related protein (LRP) and epidermal growth factor receptor (EGFR) expression. Tumors positive for nuclear YB-1 and LRP had a significantly worse prognosis, and those positive for nuclear YB-1 and EGFR had a significantly worse prognosis as well. Downregulation of YB-1 with small interfering RNA demonstrated an association of these factors in vitro. Thus, YB-1, LRP, and EGFR expression are of prognostic significance in non-small-cell lung cancer.

385 Expressions of Insulin-Like Growth Factor Receptor-1 and Insulin-Like Growth Factor Binding Protein 3 in Advanced Non–Small-Cell Lung Cancer

Young Hak Kim, Shinji Sumiyoshi, Seiji Hashimoto, Katsuhiro Masago, Yosuke Togashi, Yuichi Sakamori, Chiyuki Okuda, Tadashi Mio, Michiaki Mishima

The insulin-like growth factor (IGF) pathway plays an important role in tumor progression. We examined immunohistochemical expression of both IGF receptor-1 (IGF-1R) and IGF binding protein 3 in 68 patients with advanced non-small-cell lung cancer and found that IGF-1R expression was significantly more frequent in squamous cell carcinoma (100%) than in adenocarcinoma (44%) (P < .001). IGF-1R antibody may be useful in the pathologic diagnosis in non-small-cell lung cancer.

Current Trial

391 Rationale and Design of MARQUEE: A Phase III, Randomized, Double-Blind Study of Tivantinib Plus Erlotinib Versus Placebo Plus Erlotinib in Previously Treated Patients With Locally Advanced or Metastatic, Nonsquamous, Non–Small-Cell Lung Cancer

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