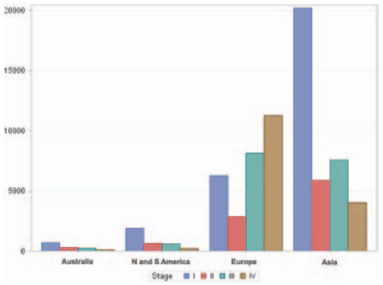
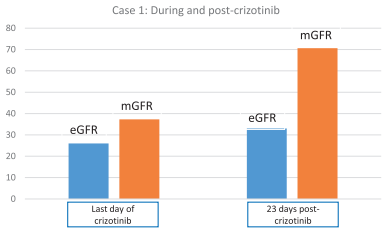
IN THIS ISSUE

- **The IASLC Lung Cancer Staging Project: The New Database to Inform the 8th Edition of the TNM Classification of Lung Cancer**



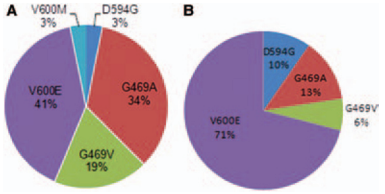
The 7th edition of the tumor, node, and metastasis (TNM) classification of lung cancer, developed as a result of retrospective database analyses of the International Association for the Study of Lung Cancer (IASLC) between 1990 and 2000, did not provide sufficient detailed data for all descriptors of the TNM components to be validated, despite the large number of lung cancer patients involved (n = 81,495). The need to address these limitations fueled the initiation of a second phase of the Lung Cancer Staging Project by the IASLC Staging and Prognostic Factors Committee. The new database included 77,156 evaluable lung cancer patients (70,967 non–small-cell lung cancer [NSCLC] and 6189 small cell lung cancer [SCLC]) diagnosed between 1999 and 2010. The data, obtained from 35 sources in 16 countries, particularly those contributed via the online electronic data capture system (n = 4667) contained all required elements for refinement analysis of the TNM descriptors. Europe is the leading contributor (n = 46,560), followed by Asia (n = 41,705); whereas North America (n = 4660) and Australia (n = 1593) presented with less cases compared with previous databases. South America contributed for the first time (n = 190). Patients predominantly received surgery alone, and fewer patients received chemotherapy alone or in combination with radiotherapy as a result of no clinical trial data in the analysis. There was a 50% decline in patients with SCLC, whereas the number of patients with NSCLC remained stable. The analysis will be based on established objectives for the TNM components to further assess the prognostic significance of (1) tumor size and the different T descriptors; (2) tumor burden in hilar and mediastinal lymph nodes; and (3) number and location of metastases, and confirmation of revised M1a and M1b of the 7th edition of the classification. The findings of these analyses and recommendations for revision will inform the 8th edition of the TNM classification, to be available in 2016. (p. 1618)

- **Crizotinib Effects on Creatinine and Noncreatinine-Based Measures of Glomerular Filtration Rate**



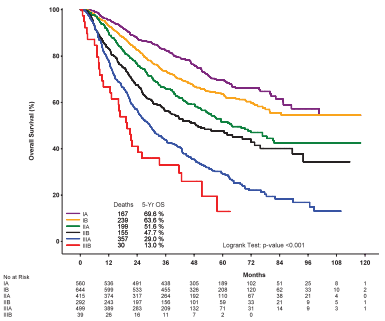
The authors sought to investigate the effects of crizotinib on the measurement of kidney function using creatinine and iothalamate-based estimates of glomerular filtration rate (GFR), and whether creatinine-based measure of kidney function is accurate in patients treated with crizotinib. The analysis of two patients with anaplastic lymphoma kinase (ALK)-positive NSCLC, one with preexisting renal impairment, demonstrated that crizotinib is associated with acute and chronic effects on kidney function. They found that chronic creatinine changes reflect a decline in the true GFR. Acute effects were observed with a decline in creatinine-based measure of the GFR but no decline in noncreatinine-based measurements, and a decrease in the true GFR that seemed more notable with preexisting renal impairment. The findings indicate that crizotinib is associated with different effects on kidney function: it could interfere with creatinine-based measurement but not affect the true GFR, or its prolonged exposure could result in a reduction in the true GFR measured by different approaches. The authors suggest that the use of a noncreatinine, for instance iothalamate, based measurement of kidney function should be considered in addition to creatinine-based assessment that show crizotinib-related changes before treatment modifications involving crizotinib and other renally excreted drugs. (p. 1634)

- **Clinical Characteristics and Course of 63 Patients with BRAF Mutant Lung Cancers**



Patients in this study were screened for *BRAF* mutations on codons V600, D594, and G460, with a parallel analysis of their characteristics and treatment outcomes to determine the clinical characteristics and course of patients with lung adenocarcinomas harboring *BRAF* mutations. Overall survival (OS) was compared with patients harboring *KRAS* and *EGFR* mutant lung adenocarcinomas with matching stage. The analysis identified 63 patients diagnosed with *BRAF* mutant cancers (2009–2013), in which 36 had V600 and 27 had non-V600 mutations. Smokers accounted for 92% of these patients; those harboring V600 mutations were more likely to be light/never smokers versus non-V600 mutations (p =0.007). Nineteen percent of early stage *BRAF* mutant cancers developed second primary lung cancer with *KRAS* mutations. In advanced cancers, a significantly better 3-year OS was observed in V600 mutant lung adenocarcinomas versus non-V600 mutant ones (24% versus 0%; $p < 0.001$). Ten of the 20 patients with advanced V600 mutant cancers received prior *BRAF* inhibitor treatment, and had favorable response (6% partial response, 30% stable disease, and 10% progressive disease). Taken together, the findings demonstrated that *BRAF* mutations (V600 and non-V600) are more predominant in smokers. Patients with advanced V600 mutant lung cancers have a prolonged survival versus non-V600 mutant cancers, and have benefited from *BRAF* targeted therapy. The authors suggested routine repeat biopsies and genetic testing for patients with early stage *BRAF* mutant cancers, who developed second primary *KRAS* mutant lung cancer. Nonetheless, larger studies are required to confirm the results. (p. 1669)

- **Lungscape: Resected NSCLC Outcome by Clinical and Pathologic Parameters**



This report describes the results of the Lungscape project, which was aimed to facilitate studies on the outcome of clinically, pathologically, and molecularly characterized resected NSCLC. Fully annotated tissue samples (stages I–III NSCLC) were available from a decentralized biobank, contributed by selected participating centers based on their number of patients, tissue microarray facility, and documented ethical approval. Selected patients would have comprehensive clinical data, radical resection between 2003 and 2009 with sufficient follow-up, and formalin-fixed tissue with sufficient quantity and quality. Analysis of the 2449 patients from 15 centers showed that the 5-year OS decreased with stage: 69.6% and 63.6% for stages IA and IB, 51.6% and 47.7% for stages IIA and IIB, and 29.0% and 13.0% for stages IIIA and IIIB, respectively ($p < 0.001$). Median and 5-year relapse-free survival (RFS) of 52.8 months and 47.3%, respectively were observed. Distant relapse occurred in 44.4% of patients whereas local relapse in 26.0%; 16.9% had both. Multivariate analysis demonstrated that performance status and pathological stage were significantly associated with OS, RFS, and time-to-relapse. These findings contributed to the first large surgical series observation on RFS and time-to-relapse in addition to OS for NSCLC surgical outcomes, and significant clinical and pathological prognostic factors. (p. 1675)