Biological markers and DNA flow cytometric analysis in radically resected patients with non-small cell lung cancer. A study of the Perugia Multidisciplinary Team for Thoracic Tumors

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ABSTRACT

Aims and background. The aim of this study was to evaluate the relationship between a panel of biological markers (p53, Bcl-2, HER-2, Ki67, DNA ploidy and S-phase fraction) and clinical-pathological parameters and its impact on outcome in non-small cell lung cancer (NSCLC) .

Methods and study design. Tumor tissue specimens obtained after surgical resection were collected from consecutive patients with NSCLC. We used an immunocytochemical technique for p53, Bcl-2, HER-2 and Ki67 analysis in fine-needle aspirates obtained from surgical samples that were also evaluated by flow cytometric DNA analysis using a FACScan flow cytometer.

Results. From April 2000 to December 2005, 136 patients with radically resected NSCLC were recruited. Median age was 66 years (range, 31-84 years), male/female ratio 117/19, ECOG performance status 0/1 127/4, stage I/II/III 76/25/35, squamous/adenocarcinoma/large-cell/mixed histology 62/49/17/8, smokers yes/no 121/11. Positivity of p53, Bcl-2, HER-2 and Ki67 was detected in 51.4%, 27.9%, 25.0% and 55.8% of the samples, respectively; 82.9% of the cases revealed aneuploid DNA histograms and 56.7% presented an S-phase fraction of more than 12%. Statistically significant associations between high Ki67 and poorly differentiated tumors ($P = 0.016$) and a smoking history ($P = 0.053$); p53 positivity and high Ki67 ($P = 0.002$); HER-2 positivity and adenocarcinoma subtype ($P = 0.015$) and presence of lymph node involvement ($P = 0.006$); and Bcl-2 positivity and squamous cell carcinoma subtype ($P = 0.058$) were observed. At univariate analysis, high Ki67 proved to be the only marker associated with disease-free survival ($P = 0.047$). After adjusting for stage, none of the examined immunocytochemical markers emerged as an independent factor for disease-free and overall survival; only pathological stage was identified as an independent prognostic factor for disease-free survival ($P = 0.0001$) and overall survival ($P = 0.0001$). In the group of 76 patients classified as TNM stage I, high Ki67 was the only marker associated with recurrence of disease ($P = 0.05$).

Conclusions. Our data do not support a relevant prognostic role of immunocytochemical markers in NSCLC, even if the Ki67 index might have particular relevance to identify patients with more aggressive tumors who are at high risk for disease relapse.