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Cancer Therapy: Clinical

Bronchopulmonary Carcinoid: Phenotype and Long-term Outcome in a Single-Institution Series of Italian Patients

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Purpose: The histologic distinction between low-grade typical and intermediate-grade atypical bronchopulmonary carcinoids basically lies on cellular differentiation, mitotic activity, and presence of "neoplastic" necrosis; at single patient level, however, none of these features enables a reliable prediction of the clinicopathologic outcome.

Experimental Design: The long-term postsurgical outcome of a single-institution series of 67 radically treated bronchopulmonary carcinoids was correlated with the tumor phenotype assessed by combining conventional histology with a panel of immunohistochemical markers exploring cell

differentiation (chromogranin, NSE, TTF1), cell turnover (Mib1), and apoptosis (Bcl2, Bax).

Results: Fifty-eight (86.6%) carcinoids were assessed as low-grade typical and nine (13.4%) were assessed as intermediate-grade atypical. The mean follow-up was of 85.13 months (range, 28-168; median, 82.0). All cases expressed neuroendocrine markers, whereas TTF1 was never expressed. At univariate analysis, tumor recurrence (n = 6) correlated significantly with the carcinoid histotype (P = 0.002) and with each of the following variables: tumor location (P = 0.01), mitotic index (P = 0.003), necrosis (P = 0.002), tumor vascular invasion (P = 0.0001), Mib1 expression (P = 0.005), Bcl2 expression (P = 0.024), and synchronous node metastasis (P = 0.028). The best cutoffs for Mib1 and Bcl2 expression (calculated by receiver operating characteristic curves) discriminating recurrent versus nonrecurrent tumors were 5.4% for Mib1 and 2.0% for Bcl2 (Mib1: sensitivity, 83%; specificity, 97%; area under curve, 0.844 ± 0.14; Bcl2: sensitivity, 83%; specificity, 65%; area under curve, 0.769 ± 0.12). By stratifying the patients according to the obtained cutoffs, significant differences emerged in the patients' disease-free survival (log-rank test: Mib1, P = 0.0001; Bcl2, P = 0.01).

Conclusions: Mib1 and Bcl2 significantly discriminate between recurrent versus nonrecurrent tumors, producing a biologically plausible, diagnostically suitable immunohistochemical pattern.

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Cancer Research	Clinical Cancer Research
Cancer Epidemiology Biomarkers & Prevention	Molecular Cancer Therapeutics
Molecular Cancer Research	Cell Growth & Differentiation