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Expression profiling of 21 biomolecules in locally advanced nasopharyngeal carcinomas of Caucasian patients.

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Source

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Abstract

BACKGROUND:

Since scarce data exist on the pathogenesis of nasopharyngeal carcinoma in Caucasian patients, we attempted to elucidate the responsible molecular pathways in this patient population.

METHODS:

Formalin-fixed paraffin-embedded tumor tissue samples from 107 patients, diagnosed with locally-advanced nasopharyngeal carcinoma and treated with chemotherapy or chemo-radiotherapy, were analyzed by immunohistochemistry for the expression of the following proteins: E-cadherin, P-cadherin, Fascin-1, Cyclin D1, COX-2, EGFR, VEGF-A, VEGF-C, VEGFR-2, VEGFR-3, ERCC1, p53, p63, Ki67, MAPT, phospho-p44/42MAPK, PTEN, phospho-AKT, phospho-mTOR, and phospho-GSK-3β. EBER status was assessed by in situ hybridization. The majority of the cases were included in tissue microarray. All stains were performed and assessed centrally by two pathologists. The median follow-up time was 76.8 (42.3 - 99.2) months.

RESULTS:

Biomolecules expressed in >90% of cases were: p53, COX-2, P-cadherin, EBER, phospho-GSK-3β, and Fascin-1. WHO II+III tumors were more frequently EBER & PTEN positive and VEGF-A negative. Advanced age was significantly associated with positive phospho-GSK-3β and ERCC1 expression; male gender with positive phospho-AKT and phospho-p44/42MAPK; and worse performance status (1 or 2) with negative Ki67, ERCC1, PTEN, and phospho-mTOR expression. Earlier disease stage was closely associated with p63, MAPT, PTEN, and Cyclin D1 positivity. Univariate Cox regression analysis highlighted Cyclin D1 as a negative prognostic factor for disease-free survival (p=0.034) and EBER as a positive one for overall survival (p=0.048). In multivariate analysis, advanced age and stage, poor performance status, and positive ERCC1 emerged as predictors of worse disease-free and overall survival, as opposed to positive phospho-mTOR. Clustering analysis defined two protein-expression groups being predictive of better overall survival (p=0.043).

CONCLUSIONS:

Our study is the first to examine the activation and interaction of established biomolecules and signaling pathways in Caucasian NPC patients in an effort to reveal new therapeutic targets.