Ann Oncol. 2013 Feb 13. [Epub ahead of print]

Molecular profile of head and neck squamous cell carcinomas bearing p16 high phenotype.

Rampias T, Pectasides E, Prasad M, Sasaki C, Gouveris P, Dimou A, Kountourakis P, Perisanidis C, Burtness B, Zaramboukas T, Rimm D, Fountzilas G, Psyrri A.

Source

Department of Surgery (Otolaryngology).

Abstract

BACKGROUND:

We sought to determine biomarker expression differences in head and neck squamous cell cancers (HNSCCs) based on p16/human papillomavirus (HPV) classification. In addition, our aim was to explore how expression of biomarkers is modulated after E6/E7 repression in $HPV16^+$ oropharyngeal cancer cells.

METHODS:

$HPV16^+$ and HPV^- HNSCC cells were infected with retroviruses expressing short hairpin RNA targeting HPV16 E6/E7. Components of the epidermal growth factor receptor (EGFR) pathway before and after E6/E7 gene silencing were analyzed by immunoblotting and qRT-PCR. Protein expression of 13 biomarkers was analyzed using AQUA on a tissue microarray (TMA). The HPV16 status was determined using HPV16 in situ hybridization (ISH).

RESULTS:

In $HPV16^+$ cells, E6/E7 silencing was associated with PTEN upregulation and reduction of phosphorylated EGFR. Tumors were classified into four categories based on the HPV and p16 status. $HPV^+/p16^+$ tumors expressed significantly higher levels of E-cadherin ($P = 0.003$), PTEN ($P = 0.004$), lower levels of PI3Kp110 and β-catenin ($P = 0.07$). There was a significant difference in overall survival (OS, $P = 0.016$) among the four subsets. The median OS was 24.83 months for $p16^-/HPV^-$ patients, 11.63 for $p16^-/HPV^+$ patients and was not reached for $p16^+/HPV^-$ and $p16^+/HPV^+$ groups.

CONCLUSIONS:

Aberrant EGFR signaling contributes to malignant conversion of $HPV16^+$ HNSCC cells. These results validate β-catenin as a distinct biomarker in $HPV^+/p16^+$ HNSCC. Wnt signaling inhibitors merit exploration in $HPV^+/p16^+$ HNSCC.