EFFECT OF HPV ON TREATMENT OUTCOME AND SURVIVAL IN OROPHARYNGEAL CARCINOMA – A SUB-GROUP ANALYSIS OF THE RANDOMIZED DAHANCA 5&7 TRIALS

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Objectives: To demonstrate the correlation between p16 overexpression and HPV in oropharyngeal carcinoma and to evaluate the prognostic impact of p16 status in a prospectively analyzed cohort of Danish oropharyngeal cancer patients.

Materials and Methods: 32 tonsillar carcinomas were arranged in a Tissue Micro Array and evaluated by IHC for p16 overexpression. HPV-16 DNA detection was done by *in situ* hybridization.

Between 1986 and 1999 The Danish Head and Neck Cancer group conducted the DAHANCA 5&7 randomized trials. In the present study 335 pre-treatment oropharyngeal tumour blocks from patients enrolled in these trials were evaluated by IHC for p16 status.

Results: 20 of 32 (62.5%) tonsillar carcinomas were HPV-16 positive and 19 of these were p16 positive (sensitivity: 0.95). 12 tumours were HPV-16 negative and 10 of these were p16 negative (specificity: 0.83). The two markers matched in 29 of 32 (90%) of the tumours.

In total 135 of 335 (40%) oropharyngeal tumours were p16 positive.

In univariate analysis, loco-regional tumour control was significantly improved for p16 positive tumours with 5-year actuarial values of 67% versus 36%, $p < 0.0001$. A similar beneficial outcome for p16 positive tumours was observed for cancer specific survival (69% versus 35%, $p < 0.0001$) and overall survival (54% versus 18%, $p < 0.0001$).

In multivariate analysis p16 overexpression remained a very strong independent prognostic factor for loco-regional tumour control [OR: 0.35 (95% C.I. 0.24–0.51)], cancer specific death [OR: 0.28 (0.18–0.42)] and overall death [OR: 0.33 (0.24– 0.46)] respectively. p16 was an even stronger prognostic factor related to these outcomes than T-stage and Nodal-status.

Conclusions: p16 overexpression proved to be the strongest independent prognostic factor related to survival and loco-regional tumour control in our study and so we conclude that HPV infection is significantly correlated to improved prognosis and response to radiotherapy in oropharyngeal cancer patients.