

Head & Neck Cancer: HPV Discussion

Lisa Licitra
Head and Neck Medical Oncology Unit
Fond. IRCCS Istituto Nazionale dei Tumori
Milano, Italy

Disclosures

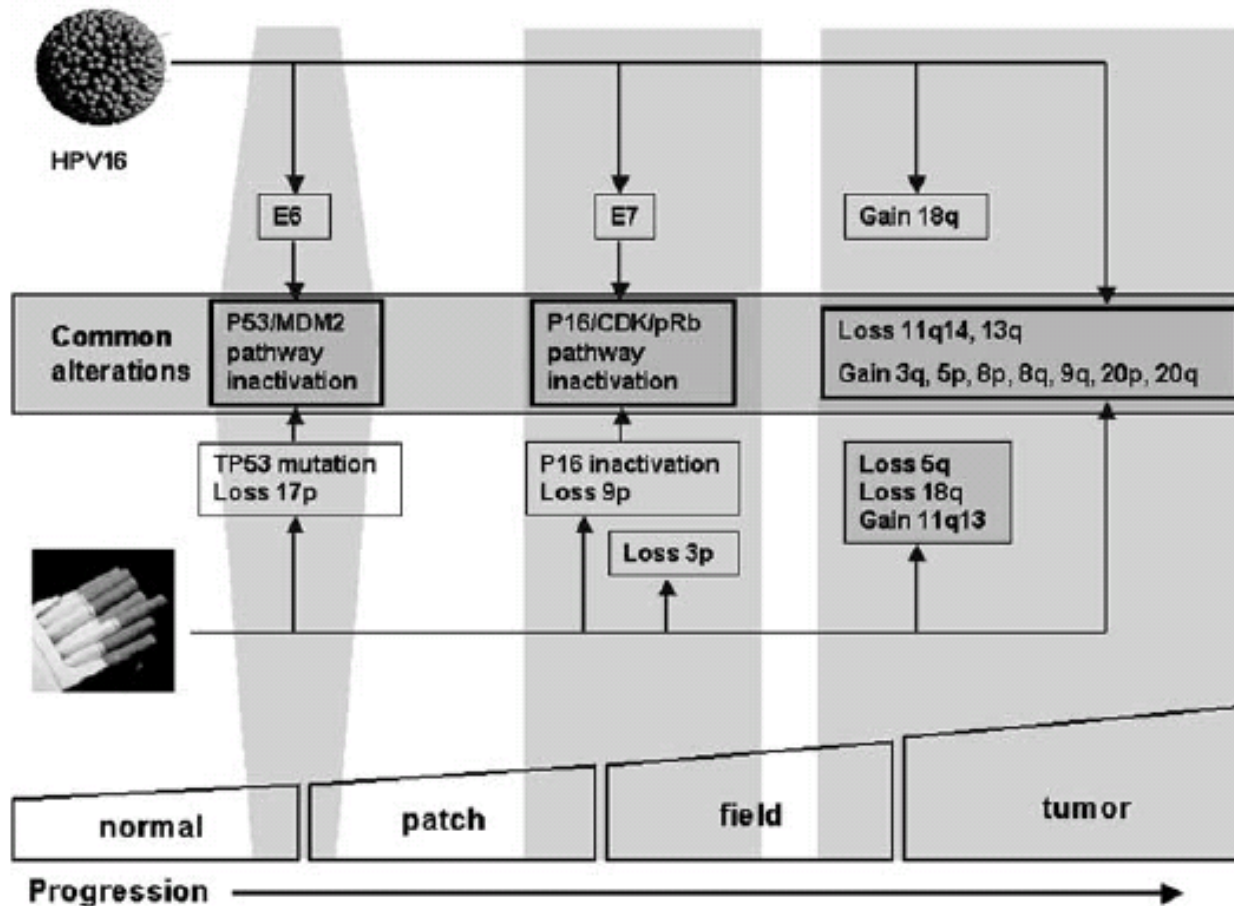
No potential conflicts of interest declared

IARC 2009

Group 1 agent	Cancers for which there is sufficient evidence in humans	Other sites with limited evidence in humans	Established mechanistic events
Epstein-Barr virus (EBV)	Nasopharyngeal carcinoma, Burkitt's lymphoma, immunosuppression-related non-Hodgkin lymphoma, extranodal NK/T-cell lymphoma (nasal type), Hodgkin's lymphoma	Gastric carcinoma,* lympho-epithelioma-like carcinoma*	Cell proliferation, inhibition of apoptosis, genomic instability, cell migration
Hepatitis B virus (HBV)	Hepatocellular carcinoma	Cholangiocarcinoma,* non-Hodgkin lymphoma*	Inflammation, liver cirrhosis, chronic hepatitis
Hepatitis C virus (HCV)	Hepatocellular carcinoma, non-Hodgkin lymphoma*	Cholangiocarcinoma*	Inflammation, liver cirrhosis, liver fibrosis
Kaposi's sarcoma herpes virus (KSHV)	Kaposi's sarcoma,* primary effusion lymphoma*	multicentric Castleman's disease*	Cell proliferation, inhibition of apoptosis, genomic instability, cell migration
Human immunodeficiency virus, type 1 (HIV-1)	Kaposi's sarcoma, non-Hodgkin lymphoma, Hodgkin's lymphoma,* cancer of the cervix,* anus* conjunctiva*	Cancer of the vulva,* vagina,* penis,* non-melanoma skin cancer,* hepatocellular carcinoma*	Immunosuppression (indirect action)
Human papillomavirus type 16 (HPV-16)†	Carcinoma of the cervix, vulva, vagina, penis, anus, oral cavity, and oropharynx and tonsil	Cancer of the larynx	Immortalisation, genomic instability, inhibition of DNA damage response, anti-apoptotic activity
Human T-cell lymphotropic virus, type-1 (HTLV-1)	Adult T-cell leukaemia and lymphoma	..	Immortalisation and transformation of T cells
<i>Helicobacter pylori</i>	Non-cardia gastric carcinoma, low-grade B-cell mucosa-associated lymphoid tissue (MALT) gastric lymphoma*	..	Inflammation, oxidative stress, altered cellular turnover and gene expression, methylation, mutation
<i>Clonorchis sinensis</i>	Cholangiocarcinoma*
<i>Opisthorchis viverrini</i>	Cholangiocarcinoma	..	Inflammation, oxidative stress, cell proliferation
<i>Schistosoma haematobium</i>	Urinary bladder cancer	..	Inflammation, oxidative stress

* Newly identified link between virus and cancer. †For other types, see table 2.

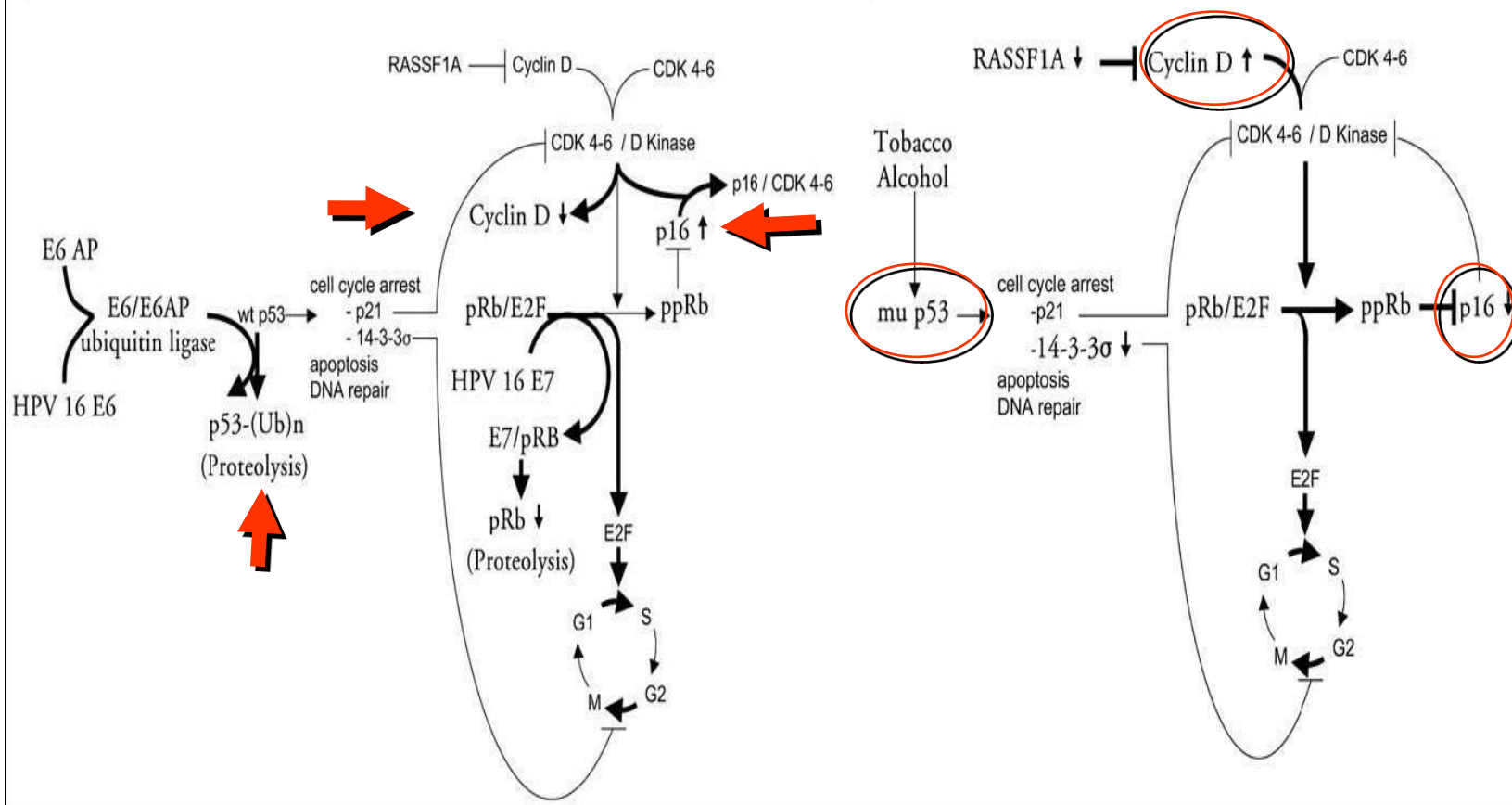
Table 1: Biological agents assessed by the IARC Monograph Working Group



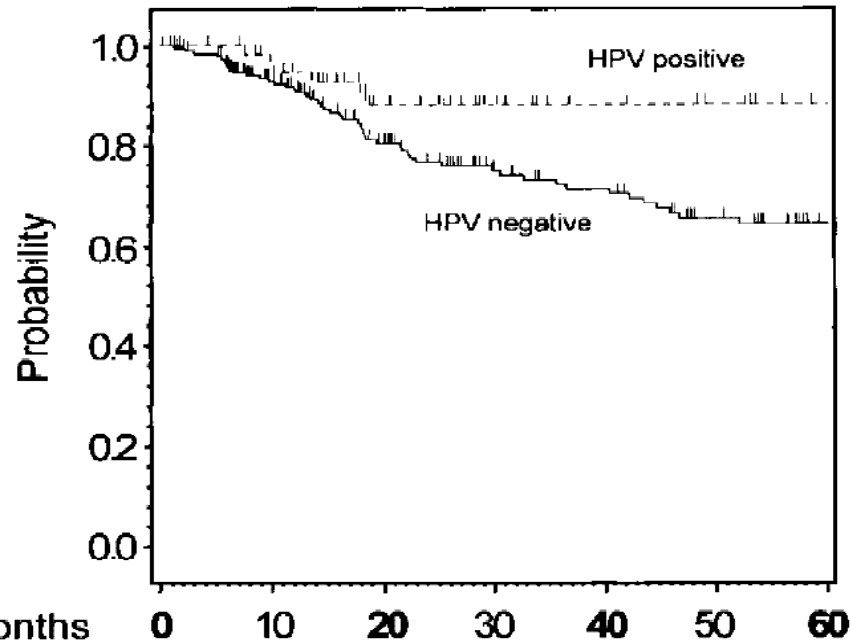
Smeets SJ Oncogene 2006

HPV-induced OSCCs

Tobacco/alcohol-induced OSCCs



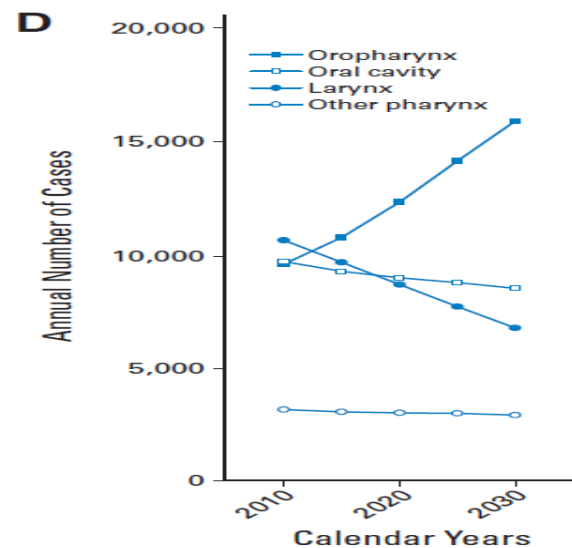
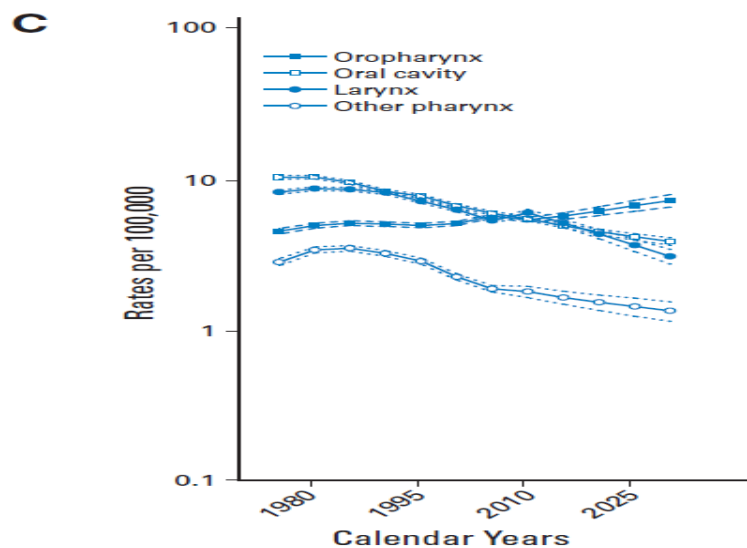
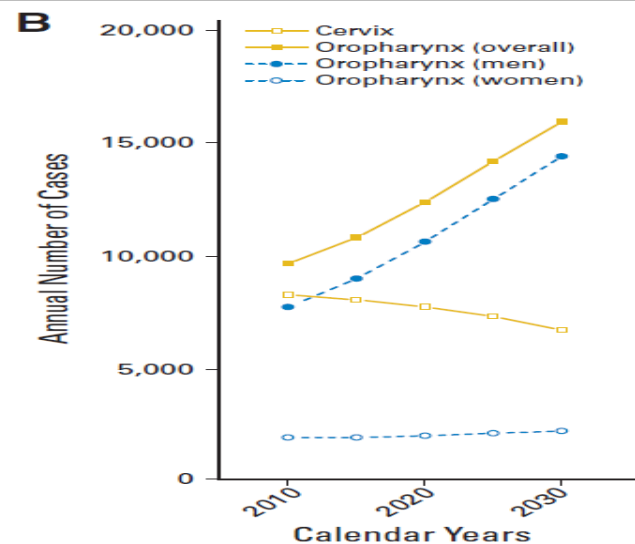
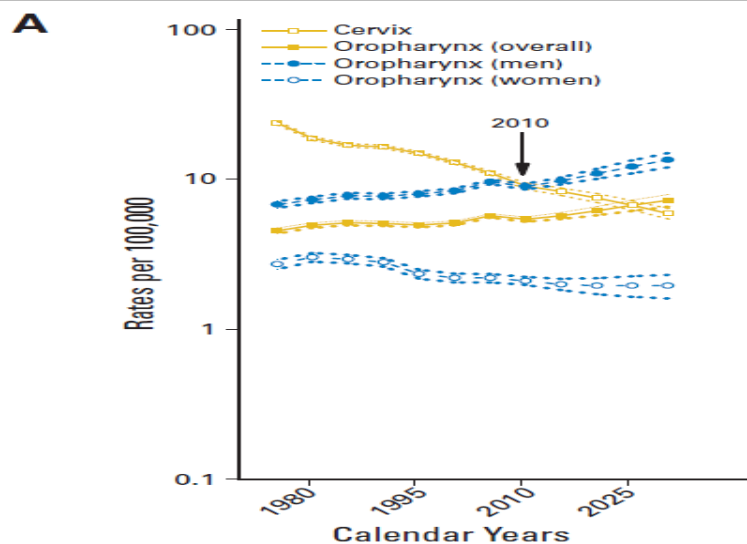
HPV as a prognostic factor

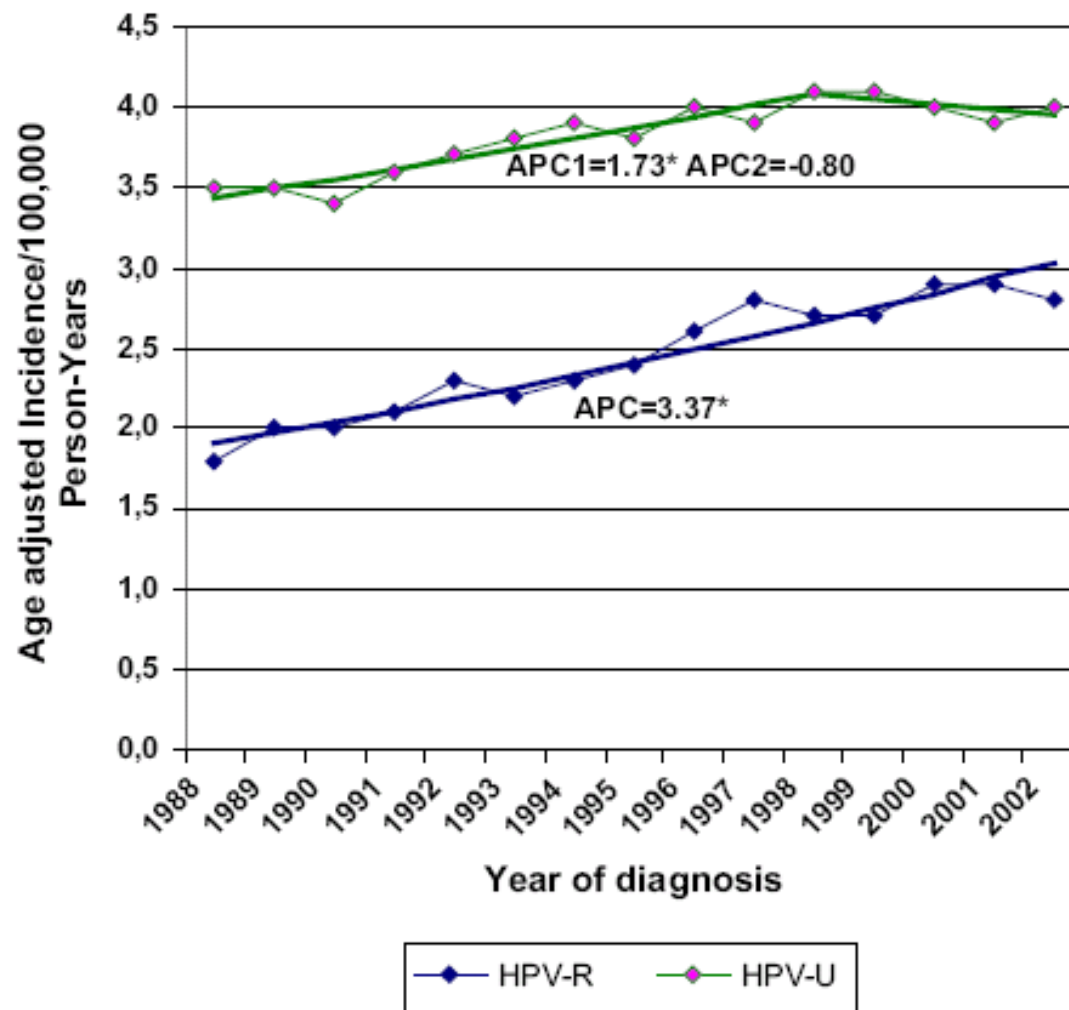


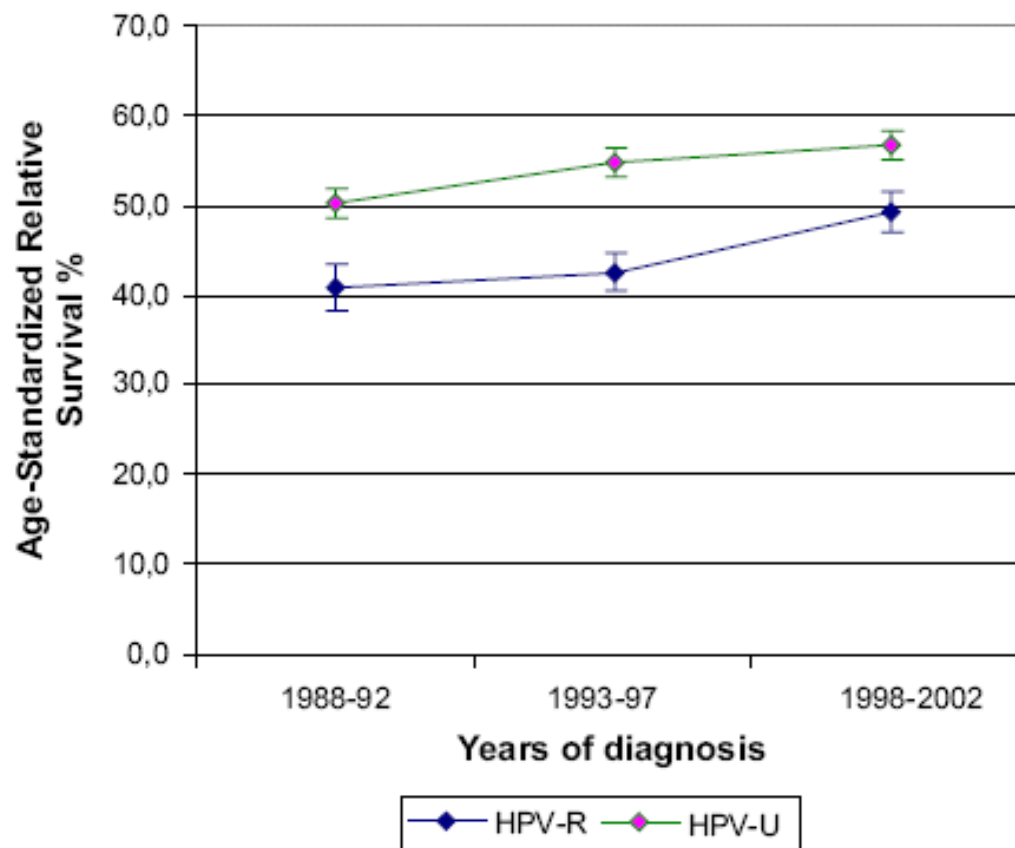
Number at risk:

HPV positive	61	37	18	10
HPV negative	191	116	75	48

Gillison, JNCI 2000







Licitra L Hematol Oncol Clin N Am 2008

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

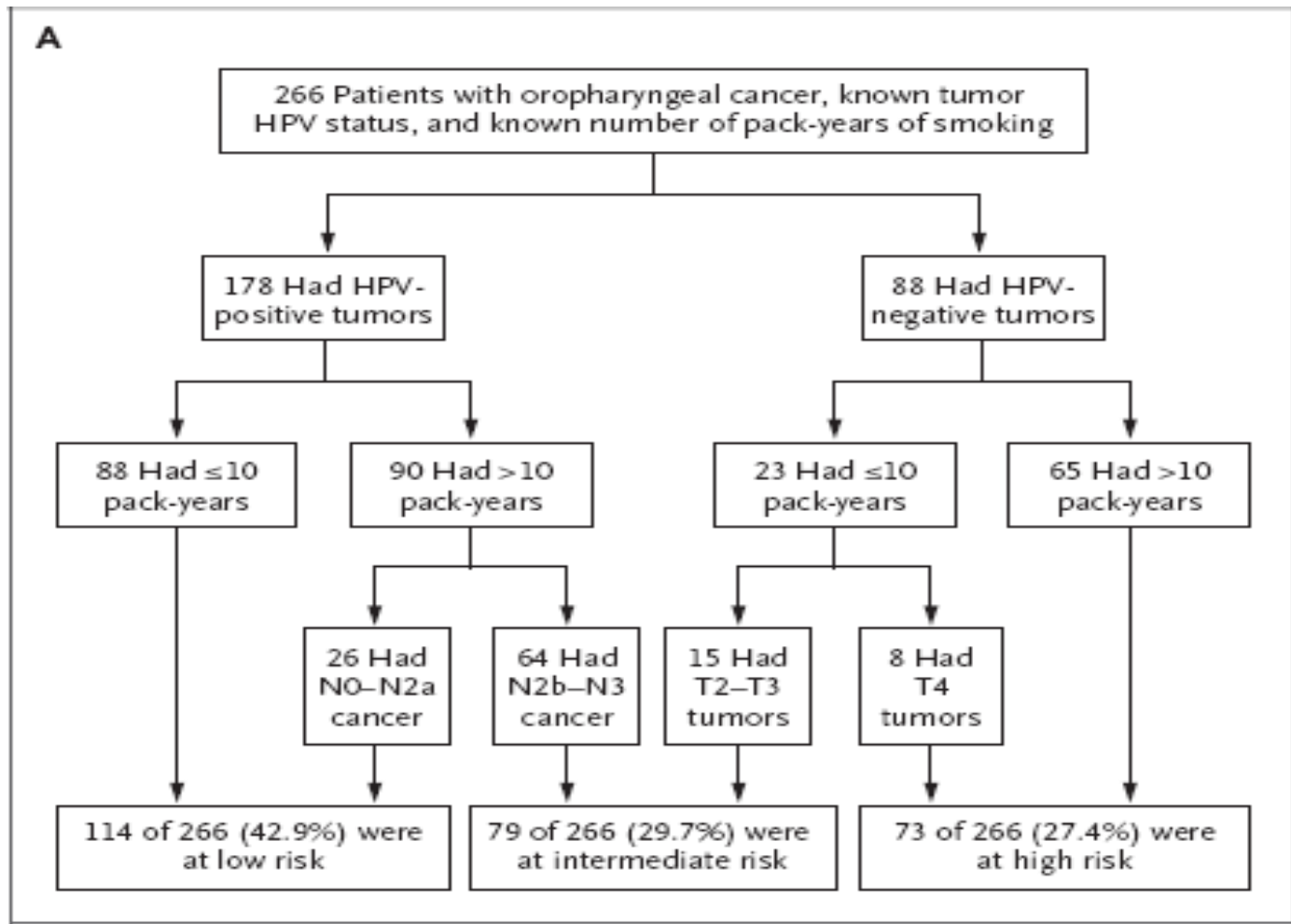
Human Papillomavirus and Survival of Patients with Oropharyngeal Cancer

K. Kian Ang, M.D., Ph.D., Jonathan Harris, M.S., Richard Wheeler, M.D.,
Randal Weber, M.D., David I. Rosenthal, M.D., Phuc Felix Nguyen-Tân, M.D.,
William H. Westra, M.D., Christine H. Chung, M.D.,
Richard C. Jordan, D.D.S., Ph.D., Charles Lu, M.D., Harold Kim, M.D.,
Rita Axelrod, M.D., C. Craig Silverman, M.D., Kevin P. Redmond, M.D.,
and Maura L. Gillison, M.D., Ph.D.

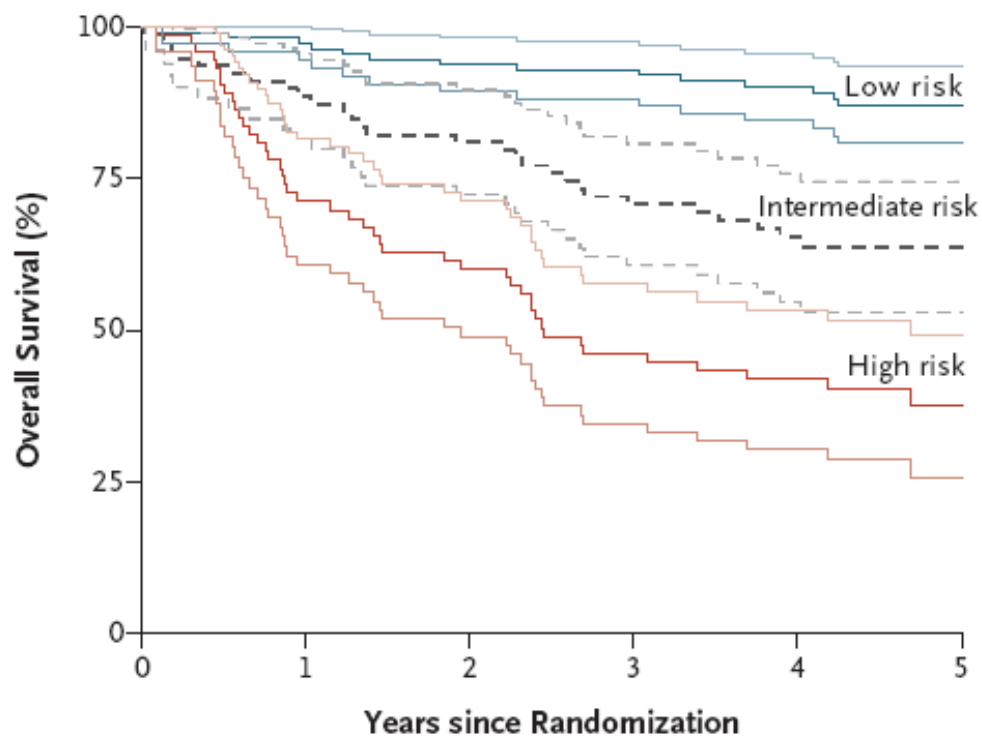
72 Gy in 42 fractions over 6 weeks + 2 cycles CDDP
vs
70 Gy in 35 fractions over 7 weeks + 3 cycles CDDP

Human Papillomavirus and survival of patients with oropharyngeal cancer

K. Ang et al.; N Eng J Med, Jun 2010



B



No. at Risk

Low risk	114	111	106	102	95	46
Intermediate risk	79	70	64	54	44	24
High risk	73	52	43	33	28	8

Gold standard tumor HPV detection

- **Traditional HPV-DNA PCR too sensitive**
- **Quantitative viral DNA or mRNA PCR more precise**
- **ISH not completely sensitive (non HPV16 HRHPVs)**
- **p16 is a surrogate marker**

ORIGINAL ARTICLE

Validation of Methods for Oropharyngeal Cancer HPV Status Determination in US Cooperative Group Trials

Richard C. Jordan, DDS, PhD, Mark W. Lingen, DDS, PhD,† Bayardo Perez-Ordóñez, MD,‡
Xin He, PhD,§ Robert Pickard, PhD,|| Michael Koluder, PhD,|| Bo Jiang, PhD,||
Paul Wakely, MD,¶ Weihong Xiao, MD,|| and Maura L. Gillison, MD, PhD||*

Am J Surg Pathol 2012

Clinical Cancer Research



Detection of Human Papillomavirus-16 in Fine-Needle Aspirates to Determine Tumor Origin in Patients with Metastatic Squamous Cell Carcinoma of the Head and Neck

Shahnaz Begum, Maura L. Gillison, Theresa L. Nicol, et al.

Clin Cancer Res 2007;13:1186-1191.

CLINICAL REVIEW

David W. Eisele, MD, *Section Editor*

Prevalence of human papillomavirus in oropharyngeal and nonoropharyngeal head and neck cancer—systematic review and meta-analysis of trends by time and region

Hisham Mehanna, PhD,^{1*} Tom Beech, MSc,¹ Tom Nicholson, MBChB,¹ Iman El-Hariry, MD, PhD,² Christopher McConkey, MSc,³ Vinidh Paleri, MS FRCS(ORL-HNS),⁴ Sally Roberts, DPhil⁵

¹Institute of Head and Neck Studies and Education, Coventry, United Kingdom, ²Synta Pharmaceuticals, Lexington, MA, USA, ³Warwick Clinical Trials Unit, Warwick Medical School, Coventry, United Kingdom, ⁴Consultant Head & Neck, Department of Otolaryngology–Head and Neck Surgery, Newcastle upon Tyne Hospitals, National Health Service Foundation Trust, Newcastle upon Tyne, United Kingdom and Honorary Clinical Senior Lecturer, Northern Institute for Cancer Research, Newcastle University, United Kingdom, ⁵School of Cancer Sciences, Birmingham Cancer Research UK Cancer Centre, College of Medical and Dental Sciences, University of Birmingham, Vincent Drive, Birmingham, United Kingdom.

Accepted 12 October 2011

Published online 20 January 2012 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/hed.22015

Table 2. Accuracy of FDG-PET/CT by Risk Stratification

Parameter	Primary		Node	
	HR	LR	HR	LR
Sensitivity, %				
PET/CT	71.4	50.0	75.0	66.7
CT	83.3	75.0	100.0	80.0
NPV, %				
PET/CT	92.0	97.8	94.7	96.3
CT	95.7	98.0	100.0	96.7
Specificity, %				
PET/CT	100.0	82.7	84.2	57.9
CT	91.7	89.1	75.0	61.7
PPV, %				
PET/CT	100.0	16.7	75.0	14.3
CT	71.4	33.3	37.5	18.2

NOTE. Accuracy parameters are tabulated for FDG-PET/CT and CT alone, divided by primary and nodal sites, for both HR and LR patients.

Abbreviations: FDG, [¹⁸F]fluorodeoxyglucose; PET, positron emission tomography; CT, computed tomography; HR, high risk; LR, low risk; NPV, negative predictive value; PPV, positive predictive value.

Take home

- **Cytology**
- **Neck SCC: seek for the primary!**
- **PET/CT**
- **Panendoscopy + biopsies**