Human Papilloma Virus Related Cancers – The changing spectrum of a preventable malignancy

Kevin Cullen, MD, Director, University of Maryland Greenebaum Comprehensive Cancer Center and Professor, University of Maryland School of Medicine

HPV Vaccination Symposium: Providers Are The Key
Saturday, March 3, 2018
What is HPV? - Epidemiology of HPV related cancers
Human papillomavirus structure

- HPV is a relatively small virus containing double-stranded DNA within a spherical shell (capsid)\(^1\)
  - The capsid is composed of two proteins, the ‘late’ or structural proteins L1 and L2\(^1\)
**HPV genome organization**

- **URR**
  - Promoter and enhancer elements
  - Viral ORI

**Early genes**
- E1—Replication
- E2—Replication and transcription
- E4—Viral release
- E5—Immune evasion
- E6—Binds p53
- E7—Binds pRB

**Late genes**
- L1—Major capsid protein
- L2—Minor capsid protein
Estimated NEW STD Infections

- HPV - 14,100,000 (71%)
- Chlamydia - 2,860,000 (14%)
- Trichomoniasis - 1,090,000 (6%)
- Gonorrhea - 820,000 (4%)
- Genital Herpes - 776,000 (4%)
- Syphilis - 55,400 (<1%)
- HIV - 41,400 (<1%)
- Hepatitis B - 19,000 (<1%)

Source: CDC's 2019 STD Fact Sheet
HPV causes more than cervical cancer

- Cervical Cancer: ~100%
- Penile Cancer: 45%
- Vulvar Cancer: ~40%
- Head & Neck Cancer: 12-70%
- Vaginal Cancer: 60-90%
- Genital Warts: ~100%
- Anal Cancer: 80+

Percentages represent cases attributable to HPV infection

References:
## U.S. Cancers Attributed to HPV

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Average # Cancers Per Year at Site (a)</th>
<th>Percent Probably Caused by HPV (a)</th>
<th>Number Probably Caused by HPV (a)</th>
<th>Percent HPV Cancers Probably Caused by HPV16 or 18 (b)</th>
<th>Number Probably Caused by HPV16 or 18 (b)</th>
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<tr>
<td>Anus</td>
<td>4,767</td>
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<tr>
<td>Cervix</td>
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<td>96</td>
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<td>76</td>
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<tr>
<td>Oropharynx</td>
<td>11,726</td>
<td>63</td>
<td>7,400</td>
<td>95</td>
<td>7,000</td>
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<tr>
<td>Penis</td>
<td>1,046</td>
<td>36</td>
<td>400</td>
<td>87</td>
<td>300</td>
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<tr>
<td>Vagina</td>
<td>729</td>
<td>64</td>
<td>500</td>
<td>88</td>
<td>400</td>
</tr>
<tr>
<td>Vulva</td>
<td>3,136</td>
<td>51</td>
<td>1,600</td>
<td>86</td>
<td>1,400</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>33,371</strong></td>
<td><strong>25,900</strong></td>
<td><strong>22,000</strong></td>
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</tr>
</tbody>
</table>


HPV Infection in the United States

- Genital warts: 25%
- Detected by colposcopy: 4%
- HPV DNA positive: Colposcopy negative: 10%
- Presence of antibodies (negative HPV test): 60%
- Not currently infected: ~75% of population exposed to HPV
High number of sexual partners
Early sexual debut
Young age
Nutrition
Genetic polymorphisms
Oral contraceptives
Chlamydia trachomatis
Smoking
Immune suppression

Sexual encounter with HPV infected partner → Acquisition of HR-HPV → Persistence of HR-HPV infection → Pre-invasive cervical lesion → Invasive cervical cancer

weeks to months → months → months to years

Primary prevention: HPV vaccination
Secondary prevention: Screening
HPV DNA testing
Cervical cytology
Americans & HPV

Americans Who Have Had HPV

Those Who Have Not
(Virgins, Nuns, Monks & People with 1 life partner)

People who got warts

Annual incidence of HPV-related cancer (.001)

Data Source: CDC
Copyright © 2013, hNews.us
Persistent infection with a number of pathogens is estimated to cause approximately 2 million cases of cancer worldwide each year (12) (see Table 4, p. 223). More than 40 percent of these cases are attributable to just four pathogens—*Helicobacter pylori*, hepatitis B virus (HBV), hepatitis C virus (HCV), and human papillomavirus (HPV).

Each pathogen is linked with a specific type of cancer or cancers, and strategies exist to eliminate or prevent infection with some of these cancer-associated pathogens (see sidebar: *Cancer-causing Pathogens: Prevention and Elimination*, p. 24). It is clear, however, that a dramatic reduction in the global incidence of these types of cancer could be achieved by more effective implementation of such strategies. Data from (43-49). Figure adapted from (34).

**HPV (30.0%)**

12 strains of human papillomavirus (HPV) caused 30% of new cancer cases attributed to infection globally in 2008.

- In the United States:
  - 90% of cervical cancer cases.
  - 50% of vaginal cancers.
  - 65% of vulvar cancers.
  - 70% of penile cancers.
  - 40% of anal cancers.
  - 45% of oropharyngeal head and neck cancers.

**HBV and HCV (29.5%)**

HBV and HCV infection caused 29.5% of new cancer cases attributed to infection globally in 2008.

- Hepatitis B virus (HBV): 40% of liver cancer deaths worldwide.
  - Over 710,000 in the United States are estimated to be infected with HBV.

- Hepatitis C virus (HCV): 35% of liver cancer deaths worldwide.
  - 2.7 million individuals in the United States are infected with HCV and unaware.

**Helicobacter pylori (32.5%)**

*Helicobacter pylori* causes:

- 32.5% of new cancer cases attributed to infection globally in 2008.
- 50% of lower gastric (stomach) cancers.
- 15% of cases of gastric mucosa-associated lymphoid tissue (MALT) lymphoma.
HPV vaccines – a remarkable success story
Richard Schlegel, M.D., Ph.D.
Papillomavirus Vaccine Development

- HPV monovalent (HPV 16) vaccine shown to protect against persistent infection 2002
- Schlegel lab (Georgetown) develops bivalent vaccine against HPV 16/18 – licensed through Medimmune to GSK
Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised controlled trial

Diane M Harper, Eduardo L Franco, Cosette Wheeler, Daron G Ferris, David Jenkins, Anne Schuind, Toufik Zahn, Bruce Innis, Paulo Naud, Newton S De Carvalho, Cecilia M Roteli-Martins, Julio Teixeira, Mark M Blatter, Abner P Kon, Wim Quint, Gary Dubin, for the GlaxoSmithKline HPV Vaccine Study Group*

Summary

Background Vaccination against the most common oncogenic human papillomavirus (HPV) types, HPV-16 and HPV-18, could prevent development of up to 70% of cervical cancers worldwide. We did a randomised, double-blind, controlled trial to assess the efficacy, safety, and immunogenicity of a bivalent HPV-16/18 L1 virus-like particle vaccine for the prevention of incident and persistent infection with these two virus types, associated cervical cytological abnormalities, and precancerous lesions.

www.lancet.com Vol 364 November 13, 2004
Findings In the according-to-protocol analyses, vaccine efficacy was 91.6% (95% CI 64.5–98.0) against incident infection and **100% against persistent infection** (47.0–100) with HPV-16/18. In the intention-to-treat analyses, vaccine efficacy was 95.1% (63.5–99.3) against persistent cervical infection with HPV-16/18 and 92.9% (70.0–98.3) against cytological abnormalities associated with HPV-16/18 infection. The vaccine was generally safe, well tolerated, and highly immunogenic.

Interpretation The bivalent HPV vaccine was efficacious in prevention of incident and persistent cervical infections with HPV-16 and HPV-18, and associated cytological abnormalities and lesions. Vaccination against such infections could substantially reduce incidence of cervical cancer.
Vaccination against human papillomaviruses shows great promise

It took almost 10 years from the discovery of an association between human papillomavirus (HPV) and cervical cancer\(^1\) to the finding of HPV type 16 in cervical cancer tissue.\(^2\) It took another 10 years to show that past infection with HPV16 increases the risk for subsequent development of invasive cervical cancer,\(^3\) and yet another decade to show that the seven most prevalent HPV types cause 87% of all cervical cancers.\(^4\) By comparison, the creation of HPV virus-like-particle (VLP) vaccines has been a rapid breakthrough. VLPs mimic the true structure of the virion and induce a striking antibody response after vaccination.\(^5\) 2 years ago, Koutsky et al\(^6\) showed that vaccination with HPV16 VLPs protected 768 vaccinated women from persistent HPV16 infection.

In today's *Lancet*, Diane Harper and colleagues now expand this rapid development in a phase 2 trial in just over 1100 participants, a study that lasted 2.5 years. VLPs of the two most important oncogenic HPV types, HPV16 and HPV18, were combined in a preventive vaccine. According-to-protocol and intention-to-treat analyses showed high efficacy for this bivalent vaccine against both the incident and persistent HPV16 and HPV18 infections. This efficacy turned out to be excellent even though the most sensitive method, vaginal self-sampling, was used to define the endpoints.
HOW DO THE THREE FDA-APPROVED HPV VACCINES DIFFER?

13

strains of HPV can cause cancer:
HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 66.

3

FDA-approved vaccines can prevent infection with some of these strains.

CERVARIX
- Protects against infection with HPV16 and HPV18.
- FDA approved in 2009.
- FDA approved for:
  - preventing cervical cancer and precancers.
  - vaccination of females ages 9 to 25.

GARDASIL
- Protects against infection with HPV16 and HPV18, as well as HPV6 and HPV11, which cause genital warts.
- FDA approved in 2006.
- FDA approved for:
  - preventing anal, cervical, vaginal, and vulvar cancers and precancers, as well as genital warts.
  - vaccination of males and females ages 9 to 26.

GARDASIL 9
- Protects against infection with HPV6, 11, 16, 18, 31, 33, 35, 52, and 58.
- FDA approved in 2014.
- FDA approved for:
  - preventing anal, cervical, vaginal, and vulvar cancers and precancers, as well as genital warts.
  - vaccination of females ages 9 to 26 and males ages 9 to 15.

American Association for Cancer Research (AACR) Cancer Progress Report 2016
Information is current as of July 2016
### 2017 Recommended Immunizations for Children 7-18 Years Old

#### Talk to your child’s doctor or nurse about the vaccines recommended for their age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Flu Influenza</th>
<th>Tetanus, diphtheria, pertussis</th>
<th>HPV Human papillomavirus</th>
<th>MenACWY</th>
<th>Pneumococcal</th>
<th>Hepatitis B</th>
<th>Hepatitis A</th>
<th>Inactivated Polio</th>
<th>MMR</th>
<th>Varicella, Mumps, Rubella</th>
<th>Chickenpox</th>
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<tbody>
<tr>
<td>7-8 Years</td>
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<td>9-10 Years</td>
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<td>11-12 Years</td>
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<td>13-15 Years</td>
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<td>16-18 Years</td>
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**More information:**
- Pregnants and adults should get a flu shot every year.
- All 11-15 year olds should get 3 doses of HPV vaccine at least 6 weeks apart. 2-3 doses are needed for those without complete vaccination by age 12 months.
- All 11-12 year olds should get 4 doses of meningococcal conjugate vaccine. 1 dose at age 11-12 years.
- Ages 16-18 years can be vaccinated with a flu vaccine.

- These shaded boxes indicate the vaccine is recommended for all children unless your doctor tells you that your child cannot safely receive the vaccine.
- These shaded boxes indicate the vaccine should be given if a child is catching up on missed vaccines.
- These shaded boxes indicate the vaccine is recommended for children with certain health or lifestyle conditions that put them at an increased risk for serious diseases. See vaccine-specific recommendations at [www.cdc.gov/vaccines/pubs/ACIP-bk.html](http://www.cdc.gov/vaccines/pubs/ACIP-bk.html).
- This shaded box indicates the vaccine is recommended for children not at increased risk but who wish to get the vaccine after speaking to a provider.
HPV Vaccine Facts
for boys and girls

Every year 26,800 women and men in the U.S. develop HPV-related cancer.

The newest HPV vaccine protects against 9 HPV types and 6 kinds of cancer.

90% of genital warts, 74% of all HPV cancers, and 81% of cervical cancers are prevented by the vaccine.

In the U.S., 79 million are currently infected with HPV. Half of all new infections are in boys and girls aged 15-24.

Up to 80% of sexually active individuals have had HPV. Safer sex practices like condoms and monogamy do not fully protect against HPV.

11-12 years is the optimal age for the vaccine because antibody production is highest, and it should be given long before any sexual contact to be most protective.

Source: CDC MMWR 2015;64(11):300-304 and CDC 2013 Surveillance
Illustration by Hannah Henry courtesy of www.thevaccinepage.org
HPV vaccination is the best way to protect your children from cancers caused by HPV.

6 out of 10 parents are choosing to get the human papillomavirus vaccine for their children.

CDC RECOMMENDS THE HPV VACCINE AT AGES 11-12
Talk to your child’s doctor about HPV cancer prevention.

www.cdc.gov/hpv
Trends in HPV Vaccination Rates: Ages 13-17 Yrs

Adolescent Vaccination Coverage, Massachusetts, NIS, 13-17 year olds, 2008 – 2015

Note: For the purposes of comparability to 2014 estimates, 2013 estimates were revised by retrospectively applying the revised 2014 provider data definition to the 2013 NIS teen data and as a result, differ from those previously published.
HPV VACCINATION IS THE BEST WAY TO PREVENT MANY TYPES OF CANCER
MANY ADOLESCENTS HAVEN'T STARTED THE HPV VACCINE SERIES

NATIONWIDE 4 OUT OF 10 GIRLS ARE UNVACCINATED

National coverage is 80%
Coverage by state:
- 40% or less
- 50-60%
- 60-80%
- 80% or greater

Percentage of adolescent girls who have received one or more doses of HPV vaccine*

NATIONWIDE 6 OUT OF 10 BOYS ARE UNVACCINATED

National coverage is 42%
Coverage by state:
- 20% or less
- 30-50%
- 40-60%
- 50% or greater

Percentage of adolescent boys who have received one or more doses of HPV vaccine*

IMPROVING HPV VACCINATION RATES WILL HELP SAVE LIVES.
A high national Tdap vaccination rate of 48% shows that it is possible to achieve high HPV vaccination coverage.

www.cdc.gov/hpv

*Estimated coverage with ≥2 doses of Human Papillomavirus (HPV) vaccine, either quadrivalent or bivalent, among adolescents aged 13-17 years.
Source: MMWR July 8, 2016.
The US cancer landscape is changing rapidly.
Head and Neck Cancer – distinct anatomic sites with distinct biology
Papillomavirus and Head and Neck Cancer

- 2/3 of oropharyngeal (tonsil and base of tongue) cancers contain detectable HPV DNA
- Almost all of these cancers associated with HPV 16
- HPV incidence increasing, now accounts for about 25% of all head and neck cancers
- Associated with other cancers as well
Oropharyngeal cancer cases in men now outnumber cervical cancer cases in women.

Chaturvedi et al. JCO 29: 4294, 2011
By 2030 there will be **four times** as many cases of oropharyngeal cancer in U.S. men as cervical cancer in U.S. women.
HPV associated head and neck cancer is climbing rapidly while smoking related head and neck cancer is declining.
Oropharyngeal Cancer - Concomitant Cisplatin/RT

Pre Treatment

Post Treatment
TAX 324: Sequential Combined Modality Therapy
TPF vs PF Followed by Chemoradiotherapy

TPF: Docetaxel \(75_{D1}\) + Cisplatin \(100_{D1}\) + 5-FU \(1000_{CI-D1-4}\) Q 3 weeks x3
PF: Cisplatin \(100_{D1}\) + 5-FU \(1000_{CI-D1-5}\) Q 3 weeks x 3
TAX324: Survival

Log-Rank P = 0.0058
Hazard Ratio = 0.70

Survival Time (months) vs. Survival Probability (%)

- TPF (n=255):
  - 67%

- PF (n=246):
  - 54%

Number of patients at risk:
- TPF: 255, 234, 196, 163, 136, 105, 72, 52, 45, 37, 20, 11
- PF: 246, 223, 169, 146, 130, 107, 85, 57, 36, 28, 10, 7
• 270 cases available (of 521)
• 269 yielded adequate DNA
• 238 interpretable HPV results
• Validation set (49 random cases repeated) error 0/49 for E6, 1/49 for E7
• 68 HPV positive, 170 HPV negative
• 59/68 positive cases oropharynx
• 49% of oropharynx HPV positive
HPV Positive Tumors Have Excellent Prognosis – TAX 324

A. \( p < 0.0001 \)

B. \( p < 0.0001 \)

All Patients  Oropharynx
RACIAL DISPARITIES IN HEAD AND NECK CANCER
“If you get cancer, whether you live or die shouldn’t be determined by your zip code.”

*Stewart Greenebaum*
All Sites – Cancer Mortality Rates 1973-2004
By Race, Males and Females

Incidence and mortality rates per 100,000 and age-adjusted to 2000 US standard population
Trends in Cancer Death Rates* by Sex and Race, US, 1975-2014

Age-adjusted to the 2000 US standard population.
Source: National Center for Health Statistics, Centers for Disease Control and Prevention
Black patients with locally advanced HNSCC show poor survival compared to whites – RTOG 9003, 9501
Black patients with locally advanced HNSCC show poor survival compared to whites – TAX 324
Cancer Prevention Research

Racial Survival Disparity in Head and Neck Cancer Results from Low Prevalence of Human Papillomavirus Infection in Black Oropharyngeal Cancer Patients

Kathleen Settle,1 Marshall R. Posner,2 Lisa M. Schumaker,1 Ming Tan,1 Mohan Suntharalingam,1 Olga Goloubeva,1 Scott E. Strome,1 Robert I. Haddad,2 Shital S. Patel,1 Earl V. Cambell III,1 Nicholas Sarlis,3 Jochen Lorch2 and Kevin J. Cullen1

Impact of Race on Survival
University of Maryland

A.

Percent Survival vs. Months

- Black
- White

Number of patients at risk:
Black: 95 63 44 28 17 14 11 8 3 3 3 3
White: 106 81 65 55 43 28 16 7 5 3 2

All Patients

p=0.009
Impact of Race on Survival
University of Maryland

A. All Patients

B. Oropharynx

p=0.009

p=0.0006
Impact of Race on Survival
University of Maryland

A. All Patients

B. Oropharynx

C. Non-Oropharynx
4am moment – “gee there is something similar about these curves....”

Oropharynx

p=0.0006

U of MD - Race

Oropharynx

p<0.0001

Tax 324 - HPV
## HPV Positive Cases by Race – TAX 324

<table>
<thead>
<tr>
<th>Race*</th>
<th>HPV negative</th>
<th>HPV positive</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>130, 66%</td>
<td>66, 34%</td>
<td>196</td>
</tr>
<tr>
<td>Black</td>
<td>28, 97%</td>
<td>1, 3%</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>158</td>
<td>67</td>
<td>225</td>
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</table>
## HPV Positive Cases by Race – TAX 324

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</tr>
</tbody>
</table>

Whites 10 times more likely than blacks to be HPV positive p=0.0003
Racial disparity is due to large number of white patients with good prognosis HPV positive tumors – rate of HPV positive tumors very low in blacks.
Findings May Explain Gap in Cancer Survival

By RONI CARYN RABIN

Scientists say they have made a discovery that may help explain the racial gap in cancer survival, providing clues to why white patients often outlive blacks even when they have what appear to be the same cancers.

The insights come from research at the University of Maryland into throat cancer and squamous-cell cancers of the head and neck, which have been increasing sharply in recent years, apparently because of the human papillomavirus — the same sexually transmitted virus that causes cervical cancer and is the target of a vaccine for girls.

The virus can also be spread through oral sex, causing cancer of the throat and tonsils, or oropharyngeal cancer.

The new research builds on earlier work suggesting that throat cancer tumors caused by the virus behave very differently from other throat cancers, and actually respond better to treatment. And the new research suggests that whites are more likely than blacks to have tumors linked to the virus, which may explain the poor outcomes of African-Americans with HPV-negative tumors.

University of Maryland researchers did the study after finding that their white patients with throat cancer were surviving 70 months on average, compared with 25 months for their black patients, even though all were treated at the same hospital.

The racial disparity in survival for oropharyngeal cancers explained most of the gap between blacks and whites for all head and neck cancers, the researchers said.

“We were shocked to see this in our own institution, where more than half of the patients we treat are African-American,” said Dr. Kevin J. Cullen, director of the Greenebaum Cancer Center at University of Maryland and senior author of the new study, in the September issue of Cancer Prevention Research.

Around the same time, the Maryland researchers were analyzing specimens of head and neck tumors gathered from participants in a treatment trial called the TAX 324 study, to determine how many tumors were linked to HPV.

The results were striking: the TAX 324 patients whose tumors were caused by the virus responded much better to treatment with chemotherapy and radiation. And they were also overwhelmingly white.

While about one-half of the white patients’ throat tumors were HPV-positive, only one of the black patients had a tumor caused by the virus, Dr. Cullen said.

“There was no difference in the survival between black and white patients in the TAX 324 trials if you subtracted out the HPV-positive patients,” he said.

The racial gap has often been explained as a result of late diagnosis among African-Americans, lack of access to care and less aggressive treatment, but experts said that in the case of oropharyngeal cancer, there appeared to be distinct biological differences between the tumors.

This suggests that the racial gap in survival for this particular cancer may trace back to social and cultural differences between blacks and whites, including different sexual practices, experts said.

At a briefing for reporters, leading cancer experts called the new report a landmark paper that would transform the treatment of oropharyngeal cancers and challenge doctors to develop new treatment options for patients with HPV-negative tumors.

Dr. Otis Brawley, medical director of the American Cancer Society, who wrote an editorial accompanying the report, said that changing sexual practices were increasing rates of head and neck cancers, and perhaps others as well.

“There is a huge public health message here,” he said.
# HPV Summary – Tax 324 and U. Maryland

<table>
<thead>
<tr>
<th></th>
<th>TAX 324</th>
<th>UMGCC OPC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HPV- (%)</td>
<td>HPV + (%)</td>
</tr>
<tr>
<td><strong>White</strong></td>
<td>130 (66)</td>
<td>66 (34)</td>
</tr>
<tr>
<td><strong>Black</strong></td>
<td>27 (96)</td>
<td>1 (4)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>157</td>
<td>67</td>
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</table>

**Combined TAX 324 + UMGCC**

<table>
<thead>
<tr>
<th></th>
<th>HPV - (%)</th>
<th>HPV+ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>White</strong></td>
<td>197 (62)</td>
<td>120 (38)</td>
</tr>
<tr>
<td><strong>Black</strong></td>
<td>99 (91)</td>
<td>10 (9)</td>
</tr>
</tbody>
</table>
HPV 16 Positive Oropharyngeal Cancer 1992-2007, University of Maryland

%HPV positive, white and black

White HPVL+  
Black HPVL+
Prognostic Markers in Oropharyngeal Cancer
Tax 324, U. of Maryland
Markers Analyzed (2)

- Bcl-2
  - Resistance to apoptosis
    - favorable prognosis
      (Dako 124)

- Thymidylate synthase
  - Resistance to 5-fluorouracil
    - adverse prognosis
      (Zymed TS 106)
Markers Analyzed (3)

- Beta-tubulin-II
  - Target of taxanes - adverse prognosis
    (Biogenex JDR 3B8)

- Her-2 neu
  - Negative prognostic factor in several cancers
    (Dako A0485)
## TAX 324 - Marker expression and survival – Univariate Analysis

<table>
<thead>
<tr>
<th>Marker's category by intensity</th>
<th>N</th>
<th>OS HR (95% CI)</th>
<th>Median (95% CI)</th>
<th>P-Value</th>
<th>OS HR (95% CI)</th>
<th>Median (95% CI)</th>
<th>P-Value</th>
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<tr>
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<tr>
<td>≤ 1</td>
<td>136</td>
<td>1.0 (0.98-1.97)</td>
<td>(39.59—)</td>
<td>0.066</td>
<td>1.0 (1.29-1.78)</td>
<td>(16.42—)</td>
<td>0.12</td>
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<tr>
<td>&gt;1</td>
<td>127</td>
<td>1.39 (1.00-1.97)</td>
<td>(41.79—)</td>
<td></td>
<td>1.29 (0.93-1.78)</td>
<td>(18.82—)</td>
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</tr>
<tr>
<td><strong>Bcl2</strong></td>
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<tr>
<td>≤ 1</td>
<td>178</td>
<td>1.0 (0.44-1.01)</td>
<td>(39.39—)</td>
<td>0.061</td>
<td>1.0 (0.70-1.02)</td>
<td>(18.53—)</td>
<td>0.06</td>
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<tr>
<td>&gt;1</td>
<td>77</td>
<td>0.67 (0.30-1.01)</td>
<td>(48.79—)</td>
<td></td>
<td>0.70 (0.48-1.02)</td>
<td>(55.82—)</td>
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<tr>
<td>≤ 1</td>
<td>153</td>
<td>1.0 (0.70-1.44)</td>
<td>(51.55—)</td>
<td>0.96</td>
<td>1.0 (0.53-1.95)</td>
<td>(21.72—)</td>
<td>0.57</td>
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<tr>
<td>&gt;1</td>
<td>108</td>
<td>1.01 (0.70-1.44)</td>
<td>(25.95—)</td>
<td></td>
<td>0.93 (0.57-1.30)</td>
<td>(29.95—)</td>
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<tr>
<td>≤ 2</td>
<td>165</td>
<td>1.0 (1.01-2.06)</td>
<td>(70.60—)</td>
<td>0.04</td>
<td>1.0 (1.32-2.06)</td>
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<td>0.01</td>
</tr>
<tr>
<td>&gt;2</td>
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<td>1.44 (1.01-2.06)</td>
<td>(37.22—)</td>
<td></td>
<td>1.32 (0.95-1.84)</td>
<td>(19.32—)</td>
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<tr>
<td>≤ 1</td>
<td>135</td>
<td>1.0 (1.13-1.80)</td>
<td>(58.64—)</td>
<td>0.51</td>
<td>1.0 (1.04-1.45)</td>
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<td>122</td>
<td>1.13 (0.79-1.60)</td>
<td>(46.64—)</td>
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<td>1.75 (0.75-1.45)</td>
<td>(21.72—)</td>
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<tr>
<td><strong>β-tub Cytoplasmic</strong></td>
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<tr>
<td>≤ 2</td>
<td>169</td>
<td>1.0 (1.67-3.42)</td>
<td>(38.64—)</td>
<td>&lt;0.001</td>
<td>1.0 (1.69-2.77)</td>
<td>(43.17—)</td>
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<td>2.39 (1.67-3.42)</td>
<td>(18.27—)</td>
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<td>1.99 (1.43-2.77)</td>
<td>(9.82—)</td>
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TAX 324 – Beta-Tubulin-II expression and overall survival

Median survival 58 months v 18.2 months (p<0.0001)
HPV status and biomarkers define risk groups in oropharyngeal cancer

High risk HPV negative – Beta tubulin positive or 2/3 other markers positive
Conclusions

- HPV is a growing cause of cancer worldwide – in women and in men.
- 75% of the US population has been exposed to HPV, nearly 15% have active asymptomatic infection.
- The HPV vaccine is safe and effective and should be given to all children starting at age 9.
- HPV associated oropharyngeal cancer has a good prognosis but can still be lethal.
- HPV and other prognostic markers can be combined to tailor therapy.
- HPV may explain some but not all outcome disparities in head and neck cancer and is the subject of ongoing research.
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  - Carole Fakhry

- **Sanofi aventis**
  - Nick Sarlis

- **Orokawa Foundation**