Anal Cancers in HIV-positive Men and Women: Future trends, future challenges

GeSIDA
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Research grant, consultant, travel support

Vir Corporation
Research grant, consultant, stock options

Ubiome, Virion Therapeutics
Stock options

Vaccitech
Consultant

Novan
Consultant
Outline

• Scope of the problem/trends in incidence
• What’s new in primary prevention
• What’s new in secondary prevention
Distribution of cancers over time

Shiels MS et al. J Natl Cancer Inst 2011;103:753–762
Park LS et al, AIDS 2016, 30:1795–1806
Anal cancer incidence

New Cases, Deaths and 5-Year Relative Survival

<table>
<thead>
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</thead>
<tbody>
<tr>
<td>5-Year Relative Survival</td>
<td>64.3%</td>
<td>60.6%</td>
<td>58.1%</td>
<td>57.2%</td>
<td>63.7%</td>
<td>73.2%</td>
<td>67.6%</td>
<td>68.7%</td>
</tr>
</tbody>
</table>


Anal Cancer Incidence Is Increasing In Males and Females in Many Countries

Age-standardized incidence rates of anal squamous cell carcinoma by sex

Based on data from the International Agency for Research on Cancer’s Cancer Incidence in Five Continents series.


Incidence/100,000 (85% CI)

- **HIV-infected**
  - MSM 131 (109-157)
  - MSW 46 (25-77)
  - Women 30 (17-50)

Silverberg M et al. CID 2012; 54:1026-34
Recent trends in anal cancer incidence
AIDS and cancer registry match study

Fig 1. Trend in anal cancer incidence among people with HIV infection and the general population in the United States, 1996 to 2012. Dots indicate the observed incidence of anal cancer among people with HIV in the study population as a function of calendar year. The solid line is the model fitted by Joinpoint, with changes in slope for the incidence trend indicated in 2000 and 2008. The dashed line is the expected incidence in the general population standardized to reflect the demographic characteristics of the HIV population.
Standardized incidence ratios for cancer in HIV-infected people, 1996–2012

<table>
<thead>
<tr>
<th>Category</th>
<th>Observed cases</th>
<th>SIR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers</td>
<td>21294</td>
<td>1.69 (1.67–1.72)*</td>
</tr>
<tr>
<td>AIDS-defining cancers</td>
<td>6384</td>
<td>13.97 (13.63–14.32)*</td>
</tr>
<tr>
<td>Kaposi’s sarcoma</td>
<td>2269</td>
<td>498.11 (477.82–519.03)*</td>
</tr>
<tr>
<td>AIDS-defining NHLs</td>
<td>3687</td>
<td>11.51 (11.14–11.89)*</td>
</tr>
<tr>
<td>DLBCL</td>
<td>2242</td>
<td>10.31 (9.89–10.75)*</td>
</tr>
<tr>
<td>Burkitt’s lymphoma</td>
<td>435</td>
<td>20.21 (18.35–22.20)*</td>
</tr>
<tr>
<td>Unspecified NHL</td>
<td>1010</td>
<td>12.42 (11.66–13.21)*</td>
</tr>
<tr>
<td>CNS NHL†</td>
<td>528</td>
<td>152.90 (140.14–166.52)*</td>
</tr>
<tr>
<td>Cervix</td>
<td>428</td>
<td>3.24 (2.94–3.56)*</td>
</tr>
<tr>
<td>Non-AIDS-defining cancers</td>
<td>14344</td>
<td>1.21 (1.19–1.23)*</td>
</tr>
<tr>
<td>Virus-related non-AIDS-defining cancers</td>
<td>4144</td>
<td>5.39 (5.23–5.55)*</td>
</tr>
<tr>
<td>Human papillomavirus-related oral cavity or pharynx</td>
<td>297</td>
<td>1.64 (1.46–1.84)*</td>
</tr>
<tr>
<td>Anus</td>
<td>1568</td>
<td>19.06 (18.43–20.03)*</td>
</tr>
<tr>
<td>Liver</td>
<td>1104</td>
<td>3.21 (3.02–3.41)*</td>
</tr>
<tr>
<td>Merkel cell carcinoma</td>
<td>10</td>
<td>2.58 (1.24–4.74)</td>
</tr>
<tr>
<td>Vagina</td>
<td>25</td>
<td>3.55 (2.30–5.26)*</td>
</tr>
<tr>
<td>Vulva</td>
<td>151</td>
<td>9.35 (7.91–10.96)*</td>
</tr>
<tr>
<td>Penis</td>
<td>114</td>
<td>5.33 (4.39–6.40)*</td>
</tr>
<tr>
<td>Hodgkin’s lymphoma</td>
<td>875</td>
<td>7.70 (7.20–8.23)*</td>
</tr>
</tbody>
</table>

Lung: 2475 cases
Prostate: 1522 cases

Hernandez-Ramirez R. www.thelancet.com/hiv Published online August 10, 2017 http://dx.doi.org/10.1016/S2352-3018(17)
Anal cancer incidence by age-women

Rates of HPV-Associated Cancers and Age at Diagnosis Among Women in the United States, 2009–2013

People living with HIV/AIDS are living into older ages

- In 2015 it was estimated that over half of people living with HIV/AIDS (PLWHA) in the U.S. were over the age of 50 years.
- The 2011 CDC HIV Surveillance report estimates that over 311,000 PLWHA were over 50 years old in 2012.

PLWHA may be aging prematurely

- Several illnesses associated with advanced age are now common among HIV-infected individuals receiving ART
  - cardiovascular disease (CVD), liver disease, renal disease, diabetes
  - neurocognitive decline and a number of cancers
The future of HPV-related cancer in HIV-infected men and women

<table>
<thead>
<tr>
<th></th>
<th>Increased incidence of cancer</th>
<th>Decreased incidence of cancer</th>
</tr>
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<tbody>
<tr>
<td>Increasing age</td>
<td>Possibly</td>
<td></td>
</tr>
<tr>
<td>Accelerated biological aging</td>
<td>Possibly</td>
<td></td>
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<tr>
<td>Lower nadir CD4 level</td>
<td>Likely</td>
<td></td>
</tr>
<tr>
<td>Lower current CD4 level</td>
<td>Possibly</td>
<td></td>
</tr>
<tr>
<td>Time on effective ART</td>
<td></td>
<td>Possibly</td>
</tr>
<tr>
<td>Earlier initiation of ART</td>
<td></td>
<td>Possibly</td>
</tr>
<tr>
<td>Screening for and removal of HSIL</td>
<td></td>
<td>Definitely (cervical)</td>
</tr>
<tr>
<td>HPV vaccination</td>
<td></td>
<td>Likely (in the future)</td>
</tr>
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</table>
Future indicators

- Anal HPV infection
- Anal HSIL
High prevalence of anal HPV infection and HSIL in HIV+ men and women

<table>
<thead>
<tr>
<th></th>
<th>Anal HPV prevalence</th>
<th>Anal HSIL prevalence</th>
<th>Anal cancer incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-infected MSM</td>
<td>96%</td>
<td>43%</td>
<td>131/100,000</td>
</tr>
<tr>
<td>HIV-infected MSW</td>
<td>59%</td>
<td>?</td>
<td>46/100,000</td>
</tr>
<tr>
<td>HIV-infected women</td>
<td>90%</td>
<td>28%</td>
<td>30/100,000</td>
</tr>
</tbody>
</table>

Chin-Hong et al. *Ann Int Med.* 2008;149;300-6
Silverberg M et al. *CID* 2012; 54:1026-34
Conley et al. *JID* 2010; 202:1567-76
Primary prevention
The nonavalent HPV vaccine

Figure 2: HPV VLP types in the nonavalent VLP vaccine
VLPs in the bivalent, quadrivalent, and the nonavalent vaccines are shown with the proportion of neoplastic disease attributed to each group. HPV = human papillomavirus. VLP = virus-like particle.
New ACIP recommendations for HPV vaccine

• For males and females: two injections at least 6 months apart if starting at age 14 or less
• Three injections at 0,1-2 and 6 months if:
  • 15 or older
  • HIV-positive or otherwise immunosuppressed
• One dose under investigation!
ACIP recommendations for HPV vaccine in HIV+ men and women

- 9vHPV, 4vHPV or 2vHPV can be used for:
  - Vaccine is safe
  - Produces lower titers than HIV-negative individuals
  - Titers probably adequate but efficacy data are lacking
  - 3 doses for males and females 15, through age 26 years
Vaccination of HIV-positive men and women

- Safe
- Immunogenic
- Effective? (AMC 072, ACTG 5298)
ACIP recommendations for HPV vaccine in HIV+ men and women

- 9vHPV, 4vHPV or 2vHPV can be used for:
  - Vaccine is safe
  - Produces lower titers than HIV-negative individuals
  - Titers probably adequate but efficacy data are lacking
  - 3 doses for males and females 15, through age 26 years
  - FDA recently approved vaccination up to age 45 years
Secondary prevention
Digital anorectal exam (DARE!)
Who should be screened?

- All HIV-positive men regardless of sexual orientation
- All HIV-negative MSM
- Women with high-grade cervical or vulvar lesions or cancer
- All HIV+ women
- All men and women with perianal condyloma
- Solid organ transplant recipients
  - Over 25 years if immunosuppressed, inc. HIV
  - Over 40 years if immunocompetent
Treatment of HSIL

- Prevention of anal cancer
- Relief of symptoms
Treatment of anal HSIL

- Challenging due to multifocal nature, size of lesions
- Multiple procedures often needed
- High recurrence rate and incidence of new lesions
- Therapy is primarily ablative
  - hyfrecation/infrared coagulation

Does it work to prevent anal cancer?
Joel Palefsky, M.D.
Protocol chair

AMC-A01: Funded by NCI and OAR: U01 CA 121947
Screen >17,385

Enroll 5,058

Retain for 5 or more years

HIV+ Men and Women over 35
Screened for HSIL

HSIL Found

Enrolled and
Randomized

Not
Enrolled

Every 6 Months:
- Digital Rectal Exam
- Anoscopy
- Biopsy (if needed)
- Anal Swab
- Blood Sample

HSIL Removed

Cancer
Not Found

Cancer
Found

Exit Study
Referred for Evaluation
and/or Treatment

Cancer
Found

Cancer
Found

Cancer
Not Found

A study of the AIDS Malignancy Consortium
Funded by the National Cancer Institute
ANCHOR Study

As of November 1, 2018:

- 6351 screened
- 2543 enrolled
Summary

- Anal cancer is increasing in general population, will remain the most common preventable cancer in HIV+ population
Summary

Primary prevention:

- The HPV vaccine is highly efficacious and is an important tool to prevent anal cancer
  - Vaccinate age 26 and under!
  - Vaccinate all HIV+ men and women 26 and under
  - After age 26 = individual decision
Summary

Secondary prevention:

- Anal HSIL can be sought and treated in an effort to reduce the risk of anal cancer
- Do your DARE!
- Treatment can be challenging
  - Efficacy- in reduction of anal cancer not yet shown- ANCHOR study will inform us
March 4, 2019 is HPV Awareness Day!

Love is everywhere. Unfortunately, so is HPV

Over 80% of people will be infected by HPV at some point in their life. While some types of HPV may not have any symptoms and visible signs, there are a few that can harm us and our loved ones. The most harmful HPV types cause cervical, anal, oral, penile and other deadly cancers. The good news is that there are solutions. By increasing awareness and taking preventative measures, we can make the world a safer place for everyone. Together we can Give Love, Not HPV.

Download Campaign Kit