HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

HPV Infection and Newer Vaccines:
An Update

S. Tsiodras, MD, PhD
Assistant professor of Medicine & Infectious diseases
University of Athens Medical School, Greece

Hosted by Paul Webber
paul@webbertraining.com
www.webbertraining.com

April 15, 2010

Cancers Attributable to High-Risk HPV

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Total Cancers*</th>
<th>% Associated With HPV**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>12,085</td>
<td>≥50%</td>
</tr>
<tr>
<td>Vaginal/Vulvar</td>
<td>3,703</td>
<td>50%</td>
</tr>
<tr>
<td>Penile</td>
<td>4,480</td>
<td>&gt;60%</td>
</tr>
<tr>
<td>Anal</td>
<td>985</td>
<td>&gt;70%</td>
</tr>
<tr>
<td>Oral/Pharyngeal</td>
<td>10,068</td>
<td>20%</td>
</tr>
</tbody>
</table>


In Greece, every year...

580 new cases
240 deaths
from cervical Cancer

Human papilloma virus Transmission

- Sexual
  - Main
  - Subclinical infection of the partner

Incubation period
- Weeks to several months

Hosted by Paul Webber paul@webbertraining.com
www.webbertraining.com
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

Cervical Ca - HPV Prevention

1. Condoms
   - Meta-analysis - 20 studies
   - protection of approx. 70%
   - NOT complete

Manhart LE, Koutsky LA. Sex Trans Dis 2002

Table 3. Male Circumcision and the Prevalence of Human Papillomavirus (HPV) Infection.1

<table>
<thead>
<tr>
<th>HPV Genotype</th>
<th>HPV-Positive</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention</td>
<td>Control Group</td>
</tr>
<tr>
<td>All genotypes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>190/307 (61.9)</td>
<td>189/302 (62.6)</td>
</tr>
<tr>
<td>At 24 mos</td>
<td>83/233 (35.6)</td>
<td>147/287 (51.2)</td>
</tr>
<tr>
<td>Low-risk genotypes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>146/307 (47.6)</td>
<td>145/302 (48.0)</td>
</tr>
<tr>
<td>At 24 mos</td>
<td>61/233 (26.2)</td>
<td>113/287 (10.4)</td>
</tr>
<tr>
<td>High-risk genotypes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At baseline</td>
<td>117/307 (38.1)</td>
<td>112/302 (37.1)</td>
</tr>
<tr>
<td>At 24 mos</td>
<td>42/233 (18.0)</td>
<td>50/287 (27.9)</td>
</tr>
</tbody>
</table>

Davies CJ et al. (Citation). 2009; 9:123. (This study was supported by a grant from the National Cancer Institute.)

Who is at risk?

US population from 15 to 50 year old

- Abnormal cytology or colposcopy
- Subclinical infection, HPV detection by PCR
- Contact with HPV infected by sexual activity without protection
- No infection identified

About 80-90% sexual active women will have once HPV infection!!

Prevalence of high risk HPV genotypes in cervical samples

Data from screening programs in Europe

In most European countries, exposure to oncogenic HPV types occurs in women aged 15-44 yrs

1. Manhart LE, Koutsky LA. Sex Trans Dis 2002

Human papillomavirus
Anogenital infection

Epidemiology USA

- NHANES study – HPV prevalence
  - vaginal swab 1921 women
  - 37% (+)
  - 45% in women aged 20-24 yrs

JAMA 2007; 297:813

Prevalence of high risk HPV genotypes in cervical samples

Data from screening programs in Europe

In most European countries, exposure to oncogenic HPV types occurs in women aged 15-44 yrs

JAMA 2007; 297:813

Hosted by Paul Webber  paul@webbertraining.com
www.webbertraining.com
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

HPV prevalence by DNA method
3404 women (42.2±13.3 yrs)-
• 49% (95% CI: 47%-50.9%)

HPV 6, 11, 16 & 18 (+) ARRAYS

HPV (+) – associations
• younger age  p<0.001
• younger age of sexual debut  p<0.001
• current and total n of sexual partners  p<0.001
• short duration of a sexual relationship  p<0.001
• marriage / multiparity = protection  p<0.001

HPV gene expression in persistence and disease progression

Vaccination

HPV types in cervical cancer worldwide

Hosted by Paul Webber  paul@webbertraining.com
www.webbertraining.com
Cumulative incidence of CIN3+ lesions during a 10 yr f/u

1 HPV test result available at onset of f/u

Kaiser Permanente data

High levels of neutralizing antibodies in the cervix, associated with protection from HPV infection

The 2 vaccines

Comparisons

<table>
<thead>
<tr>
<th>Quadrivalent (Merck)</th>
<th>Bivalent (GSK)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Licensed in US</td>
<td>2006</td>
</tr>
<tr>
<td>VLP types</td>
<td>HPV 6/11/16/18</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>Alum</td>
</tr>
<tr>
<td>Licensed for</td>
<td>males and females</td>
</tr>
<tr>
<td>males</td>
<td>females</td>
</tr>
</tbody>
</table>

HPV - Vaccines

- 1st approval from FDA 2006
  - Merck
    - Ages 9-26
    - Cost = $360

- GSK
  - Approval EMEA 2007, FDA 2009

Hosted by Paul Webber  paul@webbertraining.com  www.webbertraining.com
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

HPV Vaccine Efficacy
Vaccine HPV Type CIN2+
According to Protocol or Per Protocol

<table>
<thead>
<tr>
<th>Vaccine/</th>
<th>Vaccine</th>
<th>Placebo</th>
<th>Vaccine Efficacy % (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV type</td>
<td>N cases</td>
<td>N cases</td>
<td></td>
</tr>
<tr>
<td>Binivalent*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 16/18</td>
<td>7346</td>
<td>4</td>
<td>93% (80–98)</td>
</tr>
<tr>
<td>HPV 18</td>
<td>6703</td>
<td>2</td>
<td>99% (93–100)</td>
</tr>
<tr>
<td>HPV 16</td>
<td>6194</td>
<td>2</td>
<td>87% (40–99)</td>
</tr>
<tr>
<td>Quadrivalent**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 16/18</td>
<td>7738</td>
<td>2</td>
<td>99% (93–100)</td>
</tr>
<tr>
<td>HPV 16</td>
<td>6647</td>
<td>2</td>
<td>98% (91–100)</td>
</tr>
<tr>
<td>HPV 18</td>
<td>7362</td>
<td>0</td>
<td>100% (87–100)</td>
</tr>
</tbody>
</table>

*Five doses (pentavalent) vs four doses (binivalent), cases counted by sex and age after 1.3 years post-vaccination, mean follow-up 2.7 years.
**Four doses (quadrivalent) vs three doses, cases counted by sex and age after 1.3 years post-vaccination, mean follow-up 2.7 years.

Gardasil efficacy and high grade lesions due to HPV 6/11/16/18 combined data 3 phase III/IV studies – ATP analysis

<table>
<thead>
<tr>
<th>CIN2+ or AIS</th>
<th>CIN3+ or AIS</th>
<th>AIS</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>98% (90–100)</td>
<td>97% (90–100)</td>
<td>100% (31–100)</td>
<td></td>
</tr>
</tbody>
</table>


Gardasil efficacy and GENITAL WARTS combined data 3 phase III/IV studies – ATP analysis

Genital warts
Number of Diagnoses STD Clinics in England and Wales1
(first, recurrent & re-registered episodes)

<table>
<thead>
<tr>
<th>Year</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1971</td>
<td>10,000</td>
<td></td>
</tr>
<tr>
<td>1974</td>
<td>20,000</td>
<td></td>
</tr>
<tr>
<td>1977</td>
<td>30,000</td>
<td></td>
</tr>
<tr>
<td>1980</td>
<td>40,000</td>
<td></td>
</tr>
<tr>
<td>1983</td>
<td>50,000</td>
<td></td>
</tr>
<tr>
<td>1986</td>
<td>60,000</td>
<td></td>
</tr>
<tr>
<td>1989</td>
<td>70,000</td>
<td></td>
</tr>
<tr>
<td>1992</td>
<td>80,000</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>90,000</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>100,000</td>
<td></td>
</tr>
</tbody>
</table>

Lacey C et al. Poster presented at EBCOG 2008, Lisbon, Portugal

End of Study

Patricia design

- 18,644 women 15-25 yrs (TVC)
- 12,989 HPV-naïve women aged 15–26 years
- 14 countries - 4 continents
- 4 visit + monthly follow-up

Interim analysis1: 14.5 months (post-dose 1)
Final analysis2: 36 months (post-dose 1)


THE LANCET

Efficacy of human papillomavirus (HPV)-15/18 A504-adjuncted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women

Interpretation: The HPV15/18 A504-adjuncted vaccine showed high efficacy against CIN2+ associated with HPV 16/18 and non-vaccine oncogenic HPV types and substantial overall effect in cohorts that are enrolled in countries with vaccination and cervical screening programmes.

Hosted by Paul Webber  paul@webbertraining.com
www.webbertraining.com
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

Efficacy against CIN2+
Due to HPV-16/18

<table>
<thead>
<tr>
<th>Population</th>
<th>Group</th>
<th>n</th>
<th>Efficacy</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total naïve</td>
<td>Cervarix</td>
<td>98</td>
<td>96-100</td>
<td>0.0001</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>97</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total naïve</td>
<td>Cervarix</td>
<td>98</td>
<td>96-100</td>
<td>0.0001</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>63</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATP</td>
<td>Cervarix</td>
<td>1</td>
<td>86-100</td>
<td>0.0001</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>53</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*CIN2+ = CIN2, CIN3, AIS, διηθητικός καρκίνος

Total efficacy against CIN2+ & CIN3+
Independent of HPV genotype (total naïve population)

<table>
<thead>
<tr>
<th>End point</th>
<th>Efficacy</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN2+ up to 50 %</td>
<td>70.2</td>
<td>54.7-70.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CIN3+ up to 70 %</td>
<td>87.0</td>
<td>84.8-87.7</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

HPV-45 is associated with cervical AdenoCa

<table>
<thead>
<tr>
<th>HPV-45-associated lesions</th>
<th>CIN3+ or AIS</th>
<th>SCC</th>
<th>ADC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>12.8</td>
<td>7.6</td>
<td>5.1</td>
</tr>
<tr>
<td>HSIL</td>
<td>23.9</td>
<td>7.7</td>
<td>2.9</td>
</tr>
<tr>
<td>LSIL</td>
<td>7.0</td>
<td>2.8</td>
<td>0.7</td>
</tr>
<tr>
<td>CIN2+</td>
<td>12.8</td>
<td>7.6</td>
<td>5.1</td>
</tr>
<tr>
<td>CIN3+</td>
<td>23.9</td>
<td>7.7</td>
<td>2.9</td>
</tr>
<tr>
<td>SCC</td>
<td>7.0</td>
<td>2.8</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Global prevalence of HPV genotypes according to cervical lesion.

GARDASIL® CIN 2/3 prevention from NON-Vaccine HPV-types

<table>
<thead>
<tr>
<th>HPV genotype</th>
<th>Group</th>
<th>n</th>
<th>Efficacy</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV-16/18</td>
<td>Cervarix</td>
<td>62</td>
<td>33%</td>
<td>6, 52</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV-31</td>
<td>Cervarix</td>
<td>8</td>
<td>70%</td>
<td>32, 88</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>27</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Quadrivalent against oncogenic other than 16/18

<table>
<thead>
<tr>
<th>HPV genotypes</th>
<th>Incident Infection</th>
<th>Persistent Infection (6m)</th>
<th>Persistent Infection (12m)</th>
<th>CIN 2/3+</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV-45</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>8.0%</td>
</tr>
<tr>
<td>HPV-31</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>55.3%</td>
</tr>
<tr>
<td>HPV-33</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>19.1%</td>
</tr>
<tr>
<td>HPV-52</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>14.7%</td>
</tr>
<tr>
<td>HPV-39</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>31.6%</td>
</tr>
</tbody>
</table>

Gardasil SPC, 13 Sept 2008
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

Immunogenicity study “Head to Head”
- **Population:** Healthy women 18-45 yrs (N=1042) - 3 age groups
- **USA**
- **Design:** Randomized (1:1), double blind study of safety / immunogenicity in 2 groups:
  - Cervarix™ (N=521)
  - Gardasil® (N=521)
- **Duration:** 7 months, follow-up until month 24
- **Vaccination scheme:**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Month 0</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervarix®</td>
<td>Cervarix®</td>
<td>Placebo</td>
<td>Cervarix®</td>
<td></td>
</tr>
<tr>
<td>Gardasil®</td>
<td>Gardasil®</td>
<td>Placebo</td>
<td>Gardasil®</td>
<td></td>
</tr>
</tbody>
</table>

Measuring antibody response
- **Pseudovirion-based neutralization assay (PBNA)**
- **NCI developed method**
- **Recommended by WHO**
- Measures «biologically significant response»
- Pseudovirions are neutral
  - Plasmid developed in human cells

Neutralizing Ab against HPV-16

Neutralizing Ab against HPV-18

Correlation - HPV Ab in cervical secretions & serum Ab

Women 18-45 yrs old

High Ab levels up to 7,3 yrs – Bivalent vaccine

Adapted from De Carvalho, N et al. 25th International Papillomavirus Conference (Abstract P-29.15), 2009.

Hosted by Paul Webber  paul@webbertraining.com
www.webbertraining.com
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

Post-Vaccination Issues

- **Anaphylaxis**
  - Some data suggests increased rates of anaphylaxis with HPV compared to meningococcal vaccine (Austriani): 2.5 vs. 0.1/100,000
  - Need to consider data in United States (26 reports to VAERS 2007-08: 13 million doses)

- **Syncope**
  - HPV vaccine associated with increased rates of fainting
  - Observe adolescents (sitting) for 15 minutes

- **Safety**
  - Cervarix® > Gardasil®
    - Local reactions at injection site
  - Compliance of 3 dose vaccination scheme similar between 2 groups:
    - ≥84% completed vaccination

Safety data

<table>
<thead>
<tr>
<th>TVC population</th>
<th>HPV</th>
<th>N = 9119 (100%)</th>
<th>HAV</th>
<th>N = 9325 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>endpoint</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Medically important AE</td>
<td>2960</td>
<td>31.8</td>
<td>3025</td>
<td>32.4</td>
</tr>
<tr>
<td>Serious AE</td>
<td>701</td>
<td>7.5</td>
<td>699</td>
<td>7.5</td>
</tr>
<tr>
<td>Serious associated AE</td>
<td>11</td>
<td>0.1</td>
<td>6</td>
<td>0.1</td>
</tr>
<tr>
<td>New cases of chronic dz</td>
<td>251</td>
<td>2.7</td>
<td>268</td>
<td>2.9</td>
</tr>
<tr>
<td>New cases of autoimmune dz</td>
<td>78</td>
<td>0.8</td>
<td>77</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Pregnancies – outcome

<table>
<thead>
<tr>
<th>TVC</th>
<th>Τελική ανάλυση</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV</td>
<td>N = 1804 (100%)</td>
</tr>
<tr>
<td>Category</td>
<td>n</td>
</tr>
<tr>
<td>Normal infant</td>
<td>1124</td>
</tr>
<tr>
<td>No outcome</td>
<td>204</td>
</tr>
<tr>
<td>Infant AE</td>
<td>21</td>
</tr>
<tr>
<td>Pregnancy termination</td>
<td>185</td>
</tr>
<tr>
<td>Spontaneous abortion</td>
<td>164</td>
</tr>
</tbody>
</table>

FDA EMEA WHO - POSITION PAPER
Reports - Vaccines are safe

Clinical experience: > 58 million doses globally of 4valent

Hosted by Paul Webber  paul@webbertraining.com
www.webbertraining.com
Efficacy in older women (24 – 45 yrs)

Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine in women aged 24–45 years: a randomised, double-blind trial


Lancet 2009; 373: 1949–57

Gardasil in Women

>26 Years Old: Questions

- Decreasing health impact of vaccination with age:
  - Prevalence of prior infection increases
  - Incidence of new infection decreases
- Vaccination becomes less cost-effective as age increases
- Most ACIP Work Group members did not support vaccination of women >26 years of age
- Await data from clinical trials, FDA, cost-effectiveness

FDA Licensure: Indications for Quadrivalent HPV Vaccine in Males

- Prevention of the following diseases caused by HPV types 6 and 11:
  - genital warts
- Approved for use in males aged 9 through 26 years

Quadrivalent HPV Vaccine Efficacy

Prevention of HPV 6, 11-related Genital Warts, Males 16-26 years

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>HPV4 nN</th>
<th>Placebo nN</th>
<th>% Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genital warts</td>
<td>3'1245</td>
<td>28'1244</td>
<td>89 (66, 98)</td>
</tr>
</tbody>
</table>

Inclusion: Analysis, per protocol efficacy population, mean follow-up 2.2 yrs, received all three doses of vaccine, ratios to vaccine type of lesions.

Ref: BLA, Presentation for V18HPV4 Meeting, Sept 9, 2009

Quadrivalent HPV Vaccine in Males?

- Little benefit to women if they have high vaccination rates
- Cost-effective?
  - Kim/Goldie model: >$100,000/QALY for most scenarios
  - Merck models (more outcomes included): <$50,000/QALY
- No data on prevention of precancerous lesions

Impact of Efficacy and Disease Outcomes on Cost Effectiveness Ratios for Male HPV Vaccination in the US

[Graph showing cost-effectiveness ratios for male HPV vaccination]

Hosted by Paul Webber  paul@webbertraining.com

www.webbertraining.com
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

State of vaccination
USA - Australia - Europe

USA immunization plan (2010)

Estimated ≥ 1 Dose HPV Vaccine Coverage, Females 13-17 Years
National Immunization Survey 2007 and 2008

Most Common Reasons Reported by Pediatricians for Vaccine Refusal/Deferral
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

Quadivalent in Australia

HPV vaccination -Europe

HPV vaccination in Germany, France & Belgium

HPV vaccination Greece

Pandemic and HPV vaccination – Data from Greece

Cervical Ca – HPV vaccines

What else should we know:
- HPV vaccines will not prevent entire range of HIV infection and all cases of cervical Ca
- HPV vaccines will not prevent other STDs e.g. HSV, HIV
- HPV vaccines will not eliminate the need for cervical cancer screening
- HPV vaccine may offer postoperative protection from recurrent disease (SGOG, Chicago 2010)

Hosted by Paul Webber  paul@webbertraining.com
www.webbertraining.com
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

Cervical Ca SCREENING ISSUES...

High vaccine coverage plus screening w PAP ↓↓ cervical Ca
FRENCH MODEL

Estimated decrease of expected annual number of cervical cancers in France after introduction of vaccination

France model:
Hypotheses used in the model: 100% vaccine efficacy against HPV 16 and 18, lifetime protection, vaccination of a cohort of 370,000 14-year-old girls.

Screening coverage 55% current situation

Screening coverage 55% + Vaccine coverage 80%

Number of cervical cancers per year

Estimated decrease of expected annual number of cervical cancers in France after introduction of vaccination

-72%

3400

*Minimum expected impact is 60% (mono-infection), up to a maximum of 72% (co-infection).

The NEW ENGLAND JOURNAL of MEDICINE
APRIL 2, 2009

HPV Screening for Cervical Cancer in Rural India

Hosted by Paul Webber  paul@webbertraining.com
www.webbertraining.com
HPV Infection and Newer Vaccines: An Update
Dr. S. Tsiodras, University of Athens Medical School, Greece
A Webber Training Teleclass

Cervical Cytologic Screening Guidelines from the American College of Obstetricians and Gynecologists, 2009.

<table>
<thead>
<tr>
<th>Age</th>
<th>Recommendation for Cytologic Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 21 yr</td>
<td>Avoid screening</td>
</tr>
<tr>
<td>21 to 29 yr</td>
<td>Screen every 2 yr</td>
</tr>
<tr>
<td>30 to 65 or 70 yr</td>
<td>May screen every 3 yr</td>
</tr>
<tr>
<td>Between 65 and 70 yr</td>
<td>May discontinue screening†</td>
</tr>
</tbody>
</table>

Vaccination against HPV-16 Oncoproteins for Vulvar Intraepithelial Neoplasia

Gemma G. Kenner, M.D., Ph.D., Marc J. P. Welker, Ph.D.,
A. Rob P. M. Valenijn, Ph.D., Margaret J. C. Louis,
Dorien M. A. Berends-van der Meer, Anna J. P.G. Vloon, Farih Essahsh,
Lorraine M. Westers, René Offee, Ph.D., Jan Wouter Driehout, Ph.D.,
Aron R. Wulfplan, Ph.D., Jaap Oostendorp, Ph.D., Geert Jan Flukuen, M.D., Ph.D.,
Spierd H. van der Burg, Ph.D., and Cornelie J. M. Milief, M.D., Ph.D.


HPV vaccines newer data...

Hosted by Paul Webber  paul@webbertraining.com
www.webbertraining.com
Conclusions

- The identification of local risk factors for HPV infection together with the new vaccines will assist control of the HPV-associated disease.
- Molecular epidemiology of the infection should continue with the introduction of newer vaccines.
- Vaccination should be encouraged.
- Therapeutic vaccines in the near future!

“A vaccine that sits on the shelf is useless”