

## Human Papillomavirus

Efficacy of the Human Papillomavirus Vaccine versus Placebo in Women Ages 13 to 25 Years of Age

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## Human Papillomavirus

- HPV is a sexually transmitted disease that infects the epithelium of skin and mucous membranes.
- The infections may be asymptomatic, produce warts, or be associated with a variety of malignant neoplasias.
- Approximately 5.5 million Americans acquire anogenital infection caused by HPV every year.
- HPV has an estimated prevalence of approximately 20-40% among sexually active 20 year old women, has an increased incidence of more than 40% in college women in the United States, and has an estimated lifetime risk for women of at least 75% for one or more genital HPV infections.

## Etiology/Risk Factors

- A significant proportion of HPV infections attributable to four strains: 6, 11, 16, and 18.
- In addition to cervical cancer, HPV types 16 and 18 cause a significant proportion of vaginal, vulvular, anal, penile, head, and neck cancers.
- The most important risk factor for progression to high-grade dysplasia is a persistent cervical infection with an oncogenic HPV type, especially HPV 16 and 18 infections.

## Patient Findings and Diagnosis

- The interval between the exposure of the HPV infection and the onset of cervical cancer is usually 10 years or greater.
- The long period of latency makes cervical cancer rare in women below 25 years of age.
- The use of Papanicolaou (Pap) testing is a screening tool for early diagnosis of cervical cancer.
- Despite the preventative effort of pap tests, over 10,000 new cervical cancers were reported in the United States in 2004.

## Treatment Options

- LEEP
- Ablative therapy
- Excisional therapy
- HPV Vaccine
  - Given the morbidity and mortality associated with oncogenic HPV infections linked to cervical cancer, an effective and well tolerated vaccine to prevent the occurrence of the HPV infection would provide a major public health advantage.

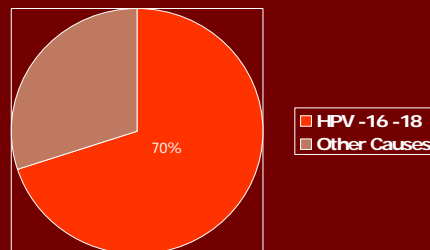
## Is the New HPV Vaccine a Good Choice for Your Daughter?



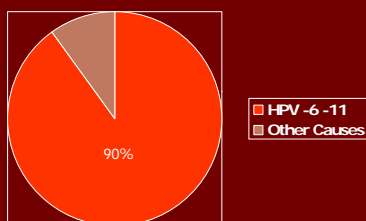
## Goals and Optimal Outcomes of Treatment

- Gardasil, a vaccine against HPV, recently became available in the U.S. for use in women 9-26 years of age.
- HPV vaccine has the potential to reduce the incidence of cervical cancer by up to 70%.

## Origin of Cervical Cancer



## Origin of Genital Warts



## Studies: HPV Vaccine v. Placebo

- Criteria for study: Per-protocol group
  - Women
  - 13-25 years of age
  - Not previously exposed to HPV
- 9 studies included in review
  - HPV vaccine compared to a placebo
  - Dosage of HPV vaccine
  - Randomized, controlled studies

## Studies: HPV vaccine v. Placebo

- Data demonstrated that a recombinant HPV -11, -16, -18, or quadrivalent L1 VLP vaccine elicited HPV-specific antibody and immunogenicity response in per-protocol group of women 13-25
- Required 2-3 dose regimen
- Most efficacious dose was 20-100µg
- 10µg dose showed less immunogenicity and took longer to reach efficacious titer levels
- Dose dependent vaccine antibody titers were found immediately following the first administration of the vaccine and all recipients had detectable proliferative responses following the administration of the second dose

## Studies: HPV Vaccine v. Placebo

- A vaccine targeted at the specific HPV pathogenic strains has the potential to impact 90% of genital wart cases, 50% of CIN 1 cases, 70% of CIN 2/3 and cervical cancer causes.
- Although some vaccines induce long-term immunity, these studies have not proven the definite length of immunity against HPV.

## Studies: HPV Vaccine v. Placebo

- Proof of vaccine efficacy complicated by the fact that the immune responses associated with protection have not been categorized
- The exact titer needed to protect against the different cancer causing strains has not been completely defined

## Studies: Conclusion

- The HPV vaccine is effective for women prior to their first exposure to the infectious strains of HPV.
- The 5.5 million cases of anogenital infections from HPV per year in the U.S. may be reduced if women are vaccinated before their first sexual experience.

## Clinical Pearls

- Gardasil Vaccine
  - Recommended for women ages 9-26
  - Does not prevent all types of cervical cancer so regular cervical cancer screening still required
  - Series of 3 injections over 6 months
    - 1<sup>st</sup> dose
    - 2<sup>nd</sup> dose – 2 months after 1<sup>st</sup> dose
    - 3<sup>rd</sup> dose – 6 months after 1<sup>st</sup> dose

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