Do We Vaccinate Older Patients: Pro

Mark H. Einstein, MD, MS, FACOG, FACS Professor and Chair Department of Obstetrics, Gynecology & Women's Health





Improving Lives Through the Prevention & Treatment of Anogenital & HPV-Related Diseases

Disclosures

Dr. Einstein has advised, but does not receive an honorarium from any companies. In specific cases his employer has received payment for his consultation from Photocure, Papivax, Inovio, PDS Biotechnologies, Natera, and Immunovaccine. If travel is required for meetings with any industry, the company pays for Dr. Einstein's travel-related expenses. Also, his employers have received grant funding for research related costs of clinical trials that Dr. Einstein has been the overall PI or local PI for the past 12 months from Astra Zeneca, Baxalta, Pfizer, Inovio, Fujiboro, Eli Lilly.



Background

- Changes in social behavior have occurred during the last 30 years
 - Older age at first marriage
 - Increase in divorce in many societies
- These changes have led to new partnering and acquisition of new sexual partners during middle age
- Literature suggests that in the US, nearly 40% of men and women have married and divorced by age 55, and that over 25% of these people have remarried at least once
- The potential for HPV infection and disease exists in women into their 30's and 40's, so it is likely that these women could benefit from prophylactic HPV vaccination





Adult Women Are At Continued Risk for

Insinga RP. *Clin Inf Dis.* 2003;36:1397-1403.

Protocol 019 – Study Description FUTURE III

- Multi-center, international study
- Randomization (1:1 ratio) to HPV4 or placebo (1:1 stratification to 24 to 34 or 35 to 45 year-olds)
- In 3,817 24- to 45-year-old women
 - No history of LEEP or hysterectomy
 - No history of biopsy-diagnosed cervical HPV disease in past 5 years
 - No history of genital warts
 - Lifetime sexual partner number not an inclusion criterion
- Pap testing and cervicovaginal sampling at ~6 month intervals for a total of 48 months

ASCCP2018 Annual Meeting

Colposcopy for ≥ASC-US



Sexual History/Marriage Status at Day 1

Paramatar	Vaccine	Placebo
Parameter	(N = 1911)	(N = 1908)
% Non-Virgins	100%	100%
Median (Range) Age at Sexual Debut (Years)	18 (5 to 39)	18 (4 to 39)
Lifetime Number of Sex Partners		
0 to 2	58%	58%
2 to 4	19%	19%
>4	23%	23%
Marital Status		
Never Married	18%	18%
Separated/Divorced	8%	7%
Widowed	1%	1%
Permanent Relationship	28%	27%
Married – first marriage	40%	42%
Married – second or higher marriage	5%	6%

Prevention of HPV 6/11/16/18-Related Cervical, Vulvar, and/or Vaginal Disease

Per Protocol Efficacy Population

Population	Vaccine		Placebo		%	95% CI
	Cases	PYR	Cases	PYR	Reduction	
All Subjects	1	2,726	13	2,682	92.4	(49.6, 99.8)
24 to 34 Year-Olds	0	1,330	8	1,316	100.0	(42.0, 100)
35 to 45 Year-Olds	1	1,396	5	1,366	80.4	(-74.9, 99.6)

PYR = person years at risk; **CI** = confidence interval.





HPV 16/18-Related Abnormal Pap Tests Protocol 019 Per Protocol Efficacy Population

HPV 16/18-Related Endpoint	Vaccine	Placebo	% Reduction	95% CI
ASC-US(HR+) or Worse	1	17	94%	63, 100
ASC-US HR(+)	1	7	86%	-10, 100
LSIL or Worse	0	11	100%	61, 100
LSIL	0	10	100%	56, 100
ASC-H	0	1	100%	
HSIL	0	0		

ASC-US = atypical squamous cells of undetermined significance; HR = high-risk; LSIL = low-grade squamous intraepithelial neoplasia; HSIL = high-grade squamous intraepithelial neoplasia; ASC-H = atypical squamous cells, cannot rule out HSIL.



Summary of Findings- Protocol 019

- Prophylactic administration of HPV4 was highly efficacious in preventing
 - HPV 6/11/16/18-related cervical, vulvar, and vaginal disease
- HPV4 induces high neutralizing antibody responses in mid-adult women
 - Anti-HPV 6, 11, 18 GMTs in 35- to 45-year-olds are ~70% of GMTs in 16to 23-year-olds

- Generally well-tolerated
 - Injection site AEs higher than placebo



FASTER Trial

- Developed to address disconnects between HPV screening and vaccination through combining both strategies with the aim of accelerating cervical cancer incident reduction
- Broadening vaccination up to age 45 paired with at least one HPV test at any age above 30 years with triage/diagnostic assessments of women who screen positive





HPV Faster Core Concept



HPV FASTER will address the following questions:

- Which is the best lifetime combination of screening and vaccination for women across all age groups
- Which combination will offer the best cost-benefit balance without compromising health
- How can we bridge inequality gaps in incidence and mortality from cervical cancer across countries





HPV FASTER controversies:

- Vaccinate women regardless of HPV status
 - Logistics and cost in knowledge of their status
- Compliance might improve if first dose given at the first HPV test, eliminating an extra visit. But does this achieve cost-balance?





Mid-adult women's attitudes about receiving the HPV Vaccine

Survey of 472 woman (≥ 25 yrs) From Augusta, Atlanta GA & San Antonio TX Recruited in community and medical settings

> Completed 46 item questionnaire, Read HPV information pamphlet Then completed 23 item post intervention questionnaire

Survey included demographic data, Attitudes about vaccines, HPV, HPV vaccines and cervical cancer

Ferris, DG et al J Lower Genital Tract Dis 2007, 11, 166-72



Mid-adult women's attitudes about receiving the HPV vaccine after educational intervention



Ferris, D.G. et al. J. Lower. Genital. Tract Dis 2007;11;166-72



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Debate in a nutshell:

Issue	Do we vaccinate older women: Pro
Is there efficacy despite prior exposure? There is efficacy for other types, which most women have NOT been exposed to	
Do older women want to be vaccinated?	
Opportunistic screening and vaccination not only in US, but globally	
Cost efficacy	Debatable given the logistics and missed opportunity concerns



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