Disclosures and Conflict of Interest

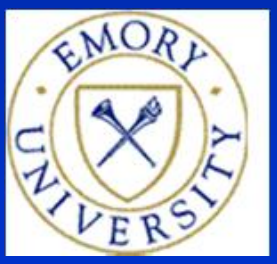
- Dr. Ault has received funding via Emory University for the conduct of HPV vaccine clinical trials with Merck.
- Dr. Ault has received funding for clinical research from Gen Probe, Roche and the NIAID.
- Dr. Ault has acted as a consultant to the NCI and the CDC, USA governmental agencies.
- Dr. Ault has also consulted with the Amercian Cancer Society.

Efficacy of HPV vaccination against the stringent-end points

Kevin A. Ault, MD

4th Helsinki Symposium on HPV Vaccination

12 January 2012



Quadrivalent HPV Vaccine (HPV4)

- Initial commercial availability in 2006
- Multiple publications in women – includes efficacy against AIS, CIN3, VIN3 (FUTURE I/II)
- Other potential end points – abnormal cytology and/or procedures
- Efficacy vs. effectiveness - herd immunity, "real world" population level effects and large scale safety surveys

Efficacy of HPV4 Vaccination

Clinical endpoint (unexposed population)	Efficacy
Cervical dysplasia	100 %
Cervical Adenocarcinoma *in situ*	100 %
Genital warts	99 %
Vulvar or vaginal dysplasia	100 %

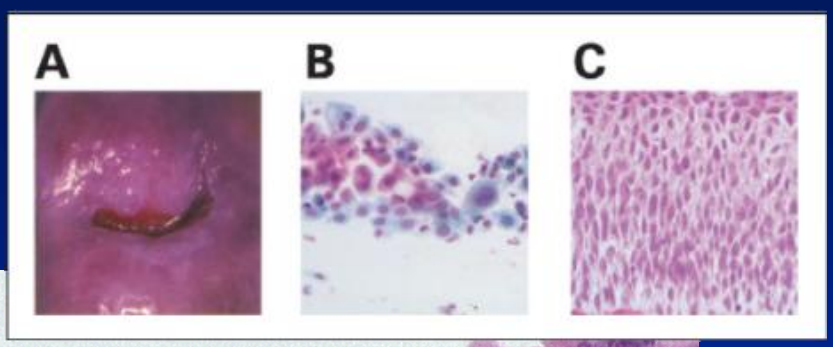
Sources – Dillner *et al.*, 2010, Ault *et al.*, 2011, and Munoz *et al.*, 2010

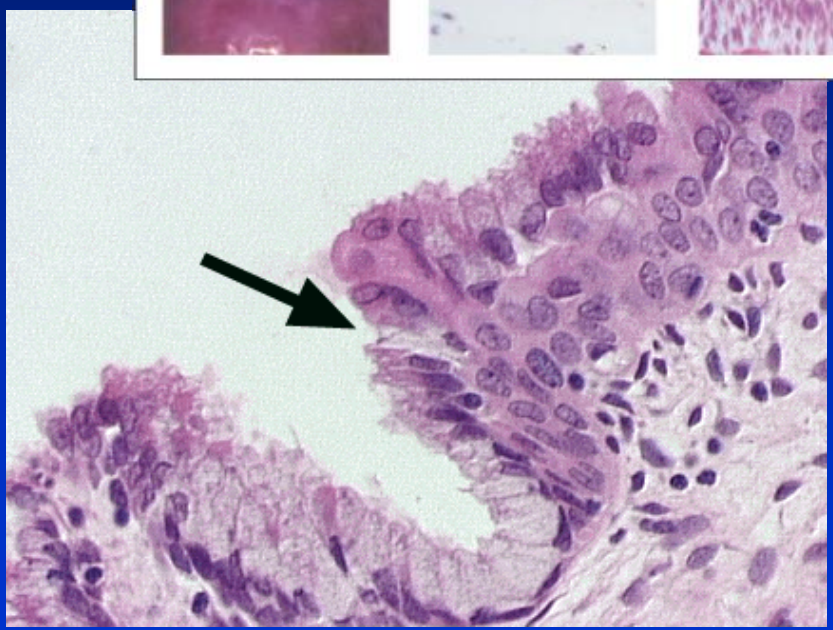
Pathology Review in HPV Vaccination Studies

- Recommended end points – CIN 2/3
- Standardized protocol involving four blinded pathologists for study biopsies
- High agreement for CIN3 and "non CIN" and also intraobserver
- Fair to moderate agreement for CIN 1 and CIN 2

Cai *et al*, 2007

Cervical Adenocarcinoma *in situ*



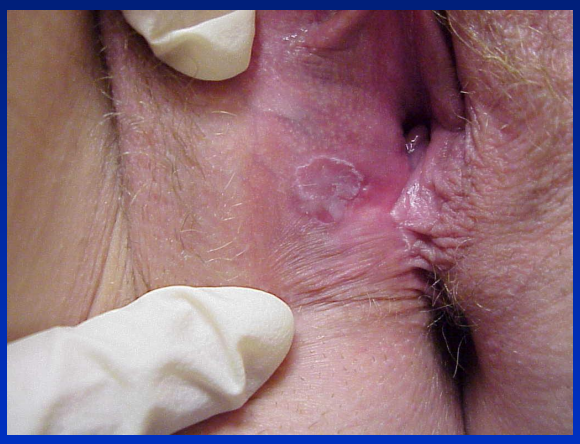


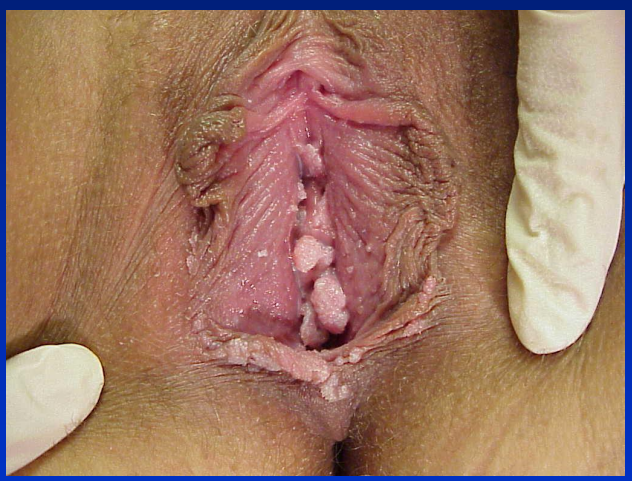
Images courtesy of Dr. Phil Castle NCI/USA

Adenocarcinoma *in situ* of uterine cervix

- Increasing incidence, difficult to diagnosis and treat, cytology insensitive
- 22 women with AIS in FUTURE I/II
- 10 % cytology indicated glandular lesion
- 50 % diagnosed during therapy for squamous disease
- 96 % due with HPV 16/18

HPV Related Vulvar Diseases - Genital Warts and VIN





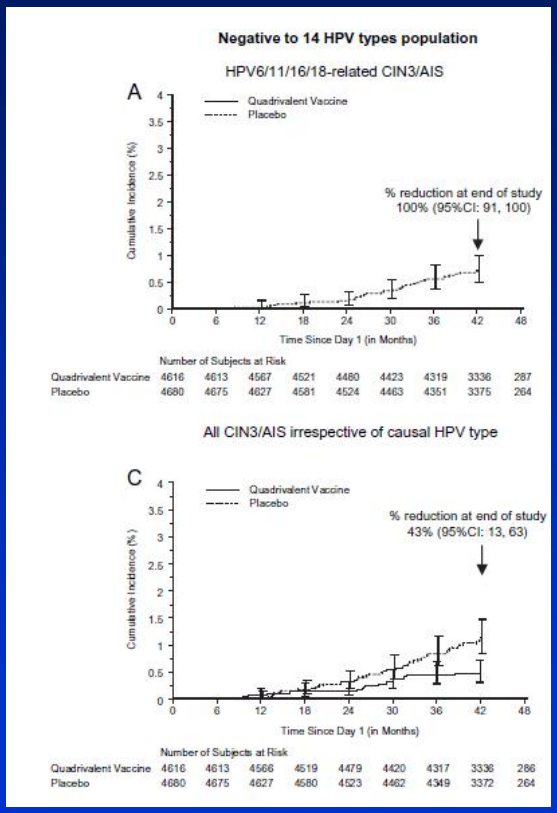
From Dr. Sebastian Faro, Houston TX USA, see also ACOG 2011

End of Study Data – HPV4

- Publication of combined FUTURE I/II
- Two large, prospective, blinded clinical trials with 17, 622 female subjects
- 24 countries with approximately 10 % from Finland
- Two cohorts described – Naïve to 14 types and "intent to treat"

Endpoint	Efficacy	95 % CI
CIN 3 due to HPV 16/18, naïve cohort	100 %	90.5 to 100 %
VaIN 2/3 or VIN 2/3 due to HPV 16, naive	94.9 %	68.3 to 99.9 %
CIN 3 due to HPV 16/18, intent to treat cohort	43.5 %	27.3 to 56.2 %
CIN 3 due to any HPV type, naive	43 %	13.0 to 63.2 %

See Munoz *et al.*, 2010



Naïve to 14 types, with 95 % tile from Munoz *et al.*, 2010

Other findings include a 10 – 40 % decrease in abnormal cytology and colposcopy/therapy

HPV4 Vaccination up to age 45

- 3, 819 women ages 24 – 45 enrolled in prospective, international, blinded trial of HPV4 vs. placebo
- Effiacy for CIN 2/3 – 83.3 %
- Underpowered to look at CIN3, AIS and VIN3

Castellsague *et al*, 2011

"Real World" Population Level Results

- Australia – school based program for HPV4 12-18 yo female adolescent with catch up to age 26
- Decrease in genital warts in women < 28 year in 2008 (Melbourne)
- Decrease in high grade cervical disease adolescent and young women (Victoria)

Fairley *et al.*, 2009, Brotherton *et al.*, 2011

The future of FUTURE II in Finland

- Linkage of Finnish volunteers ages 16-17 yo from FUTURE II study to matched cohort via Finnish Cancer Registry
- Endpoint – CIN3 +
- Follow both groups to determine population effects of HPV vaccination in adolescents

Conclusions - HPV4 Vaccine

- Multiple publications concerning disease endpoints in women – dyplasia of vulva, vagina and cervix along with genital warts
- Consistent high level of efficacy
- Evolving literature on vaccine acceptance, cost effectiveness, safety