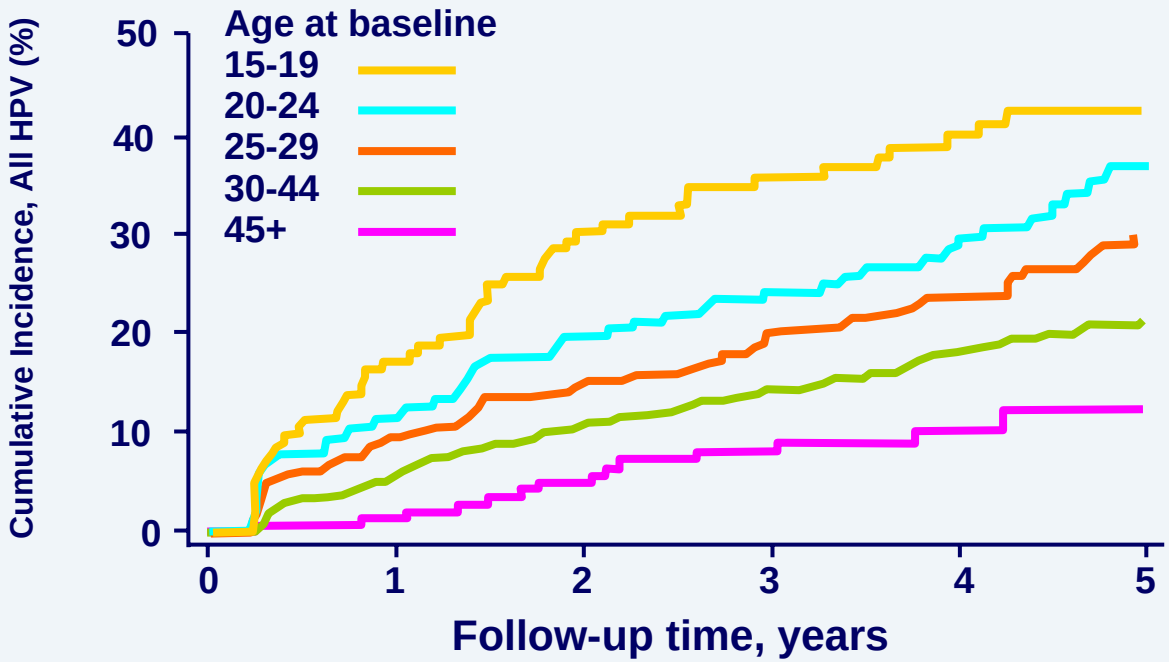
Cervarix®: GSK Cervical Cancer Candidate Vaccine Clinical Development Program in Women Over 25 Years

Gary Dubin, MD
Vice President and Director,
Clinical Development and Medical Affairs
Prophylactic Vaccines, NA
ACIP, Feb 2008

Rationale For Vaccination of Women Over 25 Years

- Majority of women over 25 years of age have not been previously infected with HPV-16 and/or HPV-18
- New HPV infections occur in sexually active women of all ages[1]



[1]Munoz, *J Infect Dis*. 2004

Rationale For Vaccination of Women Over 25 Years

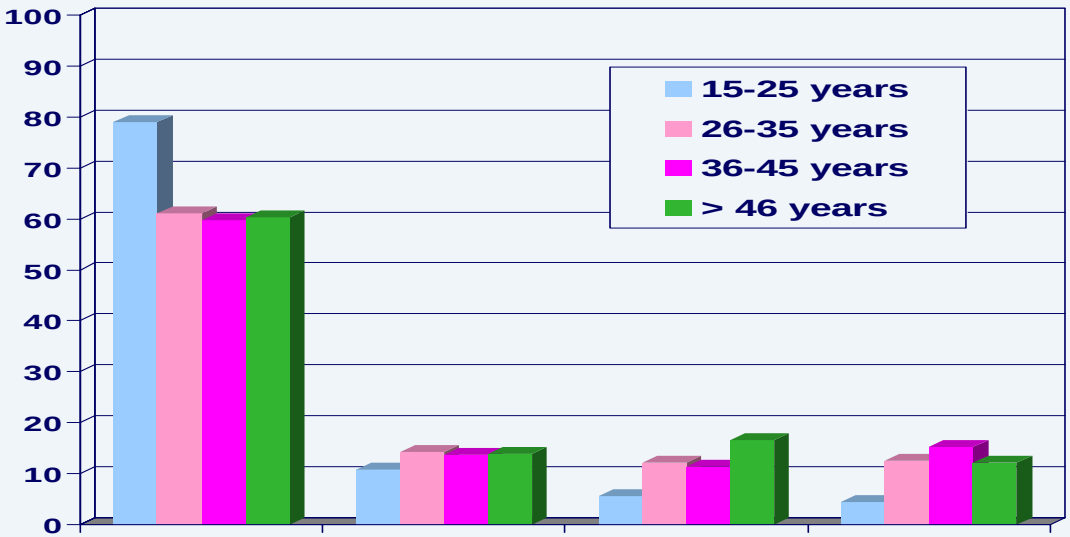
- HPV-16 or 18 non-naïve women, i.e., those with evidence of previous infection (seropositive/DNA negative) are at risk of subsequent re-infection
  - Prospective data in 15-25 year old women in control arm of GSK pivotal efficacy trial (HPV-008; mean follow-up time = 15 months)

HPV-16 Endpoint	Seronegative			Seropositive		
	N	n	Incidence rate (95%CI)	N	n	Incidence rate (95%CI)
Incident infection	7000	371	**4.56 (4.03 -5.14)**	1214	52	**3.81 (2.70 – 5.22)**
6M persistent infection	5520	144	**2.05 (1.67 – 2.48)**	800	17	**1.69 (0.89 – 2.91)**
12 M persistent infection	2972	35	**0.79 (0.52 – 1.16)**	469	7	**1.02 (0.34 – 2.32)**
CIN1+	6717	18	**0.22 (0.12 – 0.37**	1166	5	**0.35 (0.09 – 0.91)**

GSK Clinical Development Program in Women Over 25 Years

- HPV-015: Efficacy study in women >25 years (N=5751)
  - Double blind, randomized controlled multi-national study
  - Designed to evaluate efficacy against virological/CIN endpoints
  - Follow-up ongoing; interim safety analysis recently conducted

Baseline serological data (reference data in 15-25 yrs: HPV-008)



HPV-16	negative	positive	negative	positive
HPV-18	negative	negative	positive	positive

86% of women >25 years are seronegative for at least one vaccine type

Clinical Development Strategy

Girls
10-14
years

HPV-012
Immunobridge

Women
15-25
years

HPV-001/007
HPV-008

- *Efficacy against HPV-16/18 persistent infection and CIN up to 5.5 yrs*
- *Efficacy against HPV-45/31 persistent infection*

Women
26-55
years

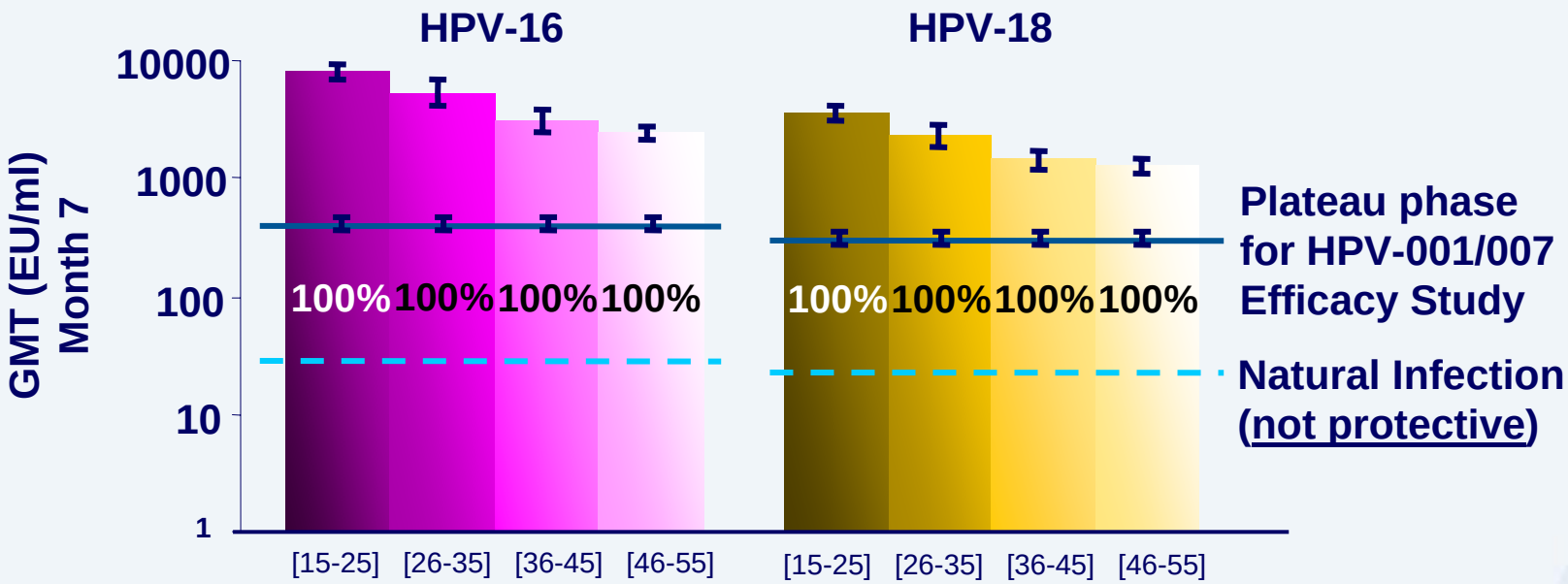
HPV-014
Immunobridge

HPV-015
Confirmatory Efficacy

[1] Harper D et al. Lancet 2006
[2] Paavonen J et al. Lancet 2007

GSK Clinical Development Program in Women Over 25 Years

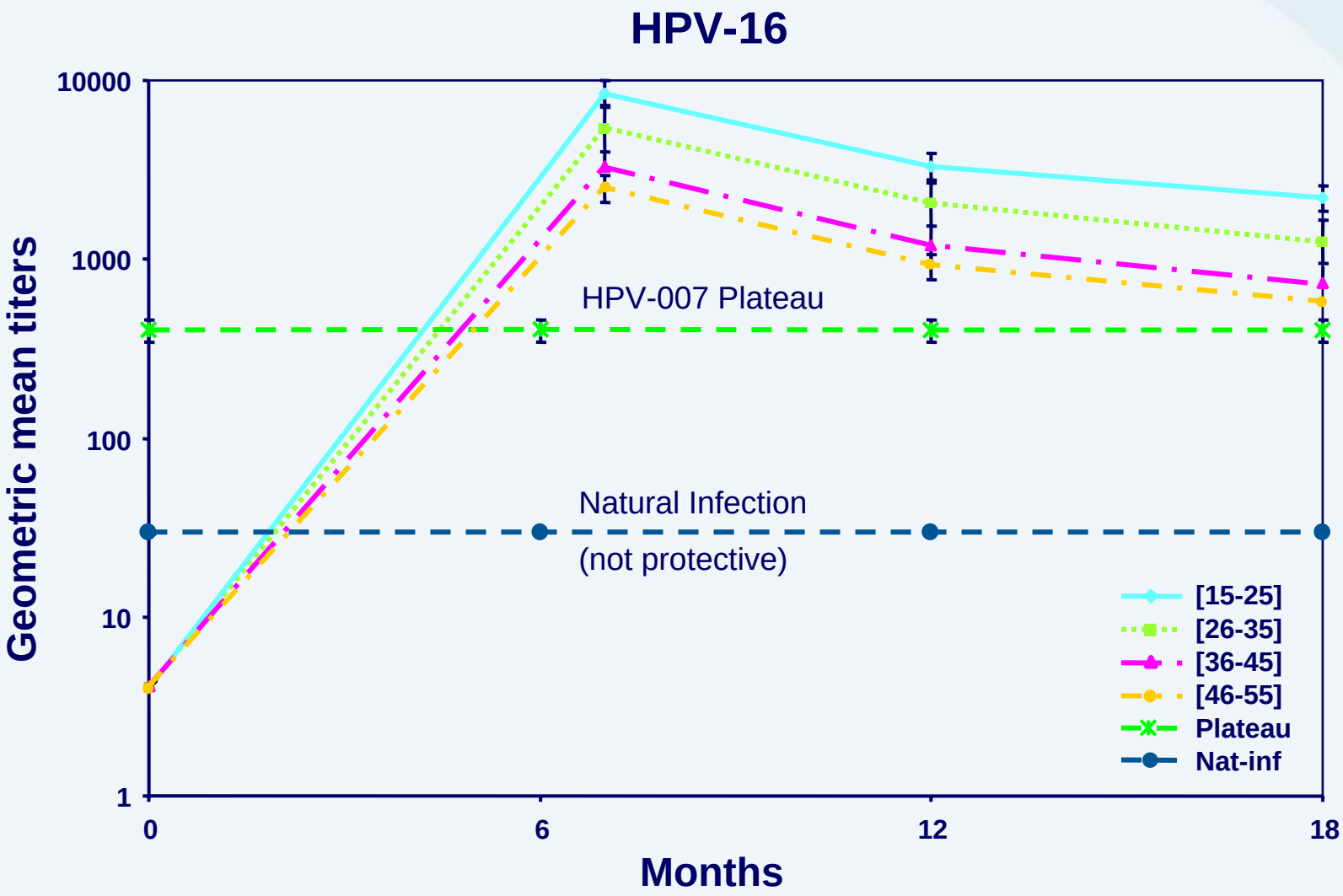
- HPV-014: Immunogenicity and safety study
  - Open, age-stratified study in Germany and Poland (N = 666)
  - Designed to compare titers in women 26-55 yrs with those in women 15-25 years
    - Efficacy previously demonstrated in women 15-25 years



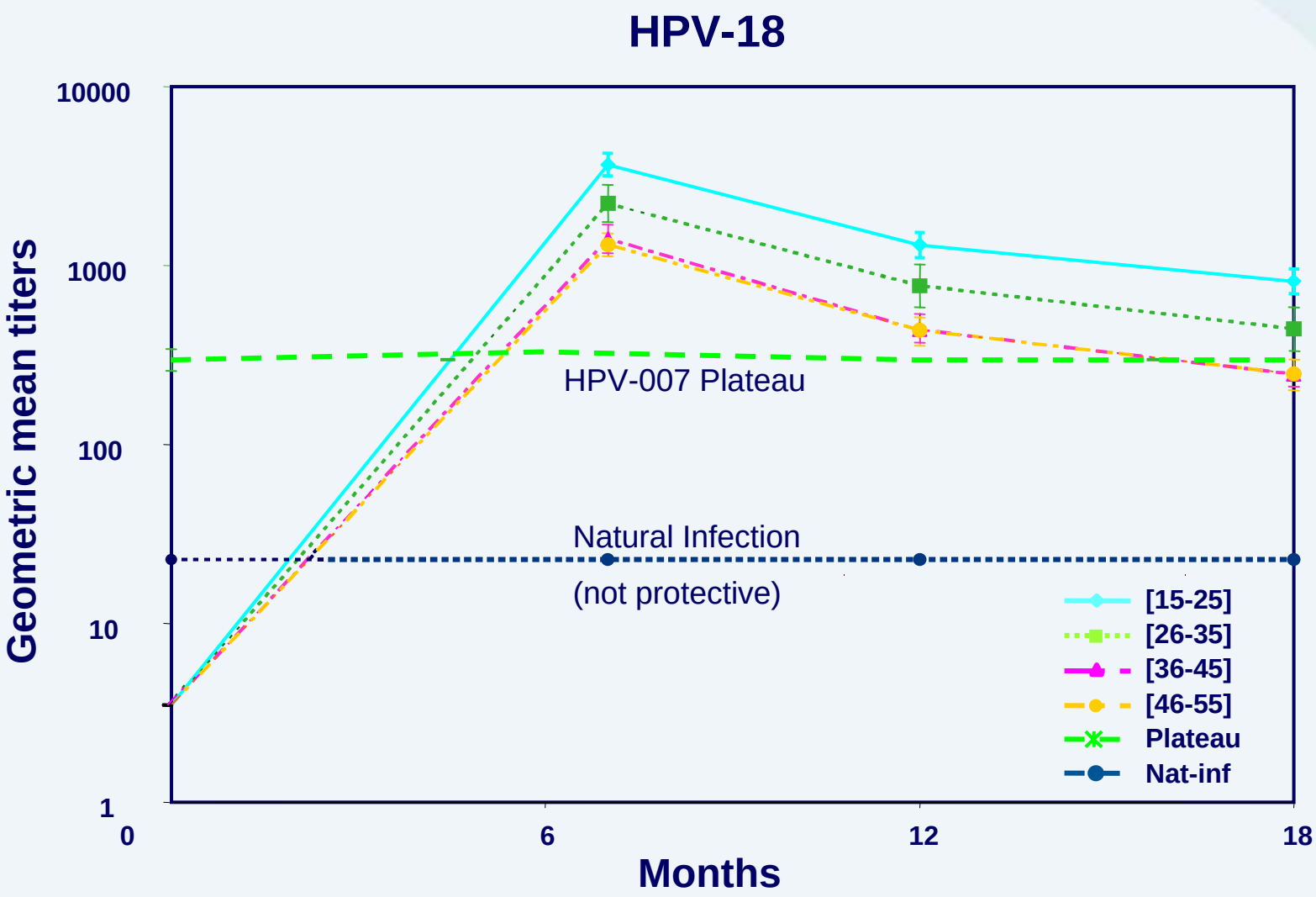
ATP cohort, Seronegative at entry

Non-inferiority of the immune response was demonstrated for both the 26-45 and 46-55 years age groups

HPV-014: Immune Response is Sustained

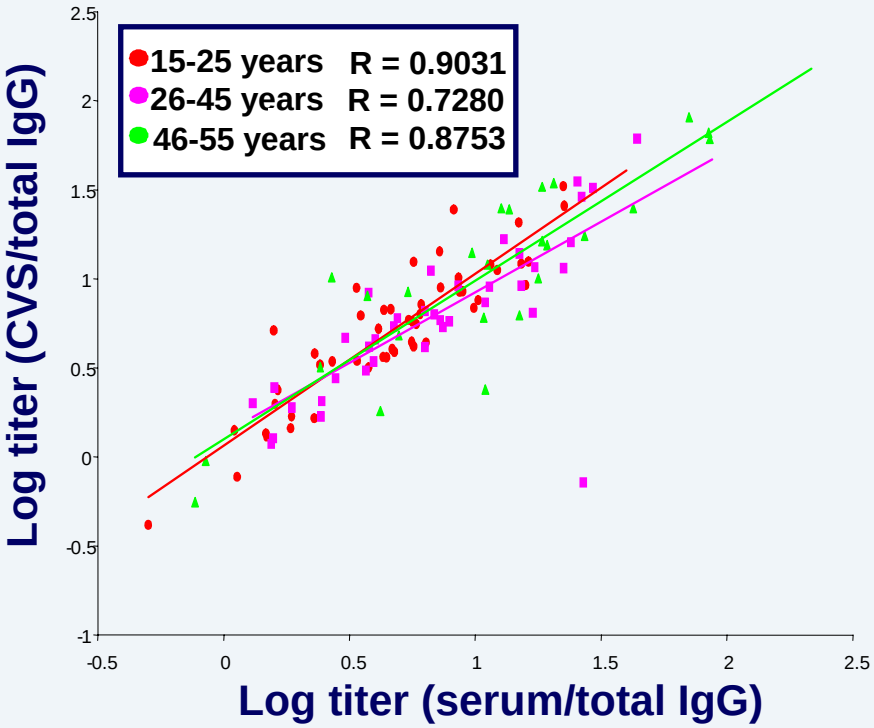


HPV-014: Immune Response is Sustained

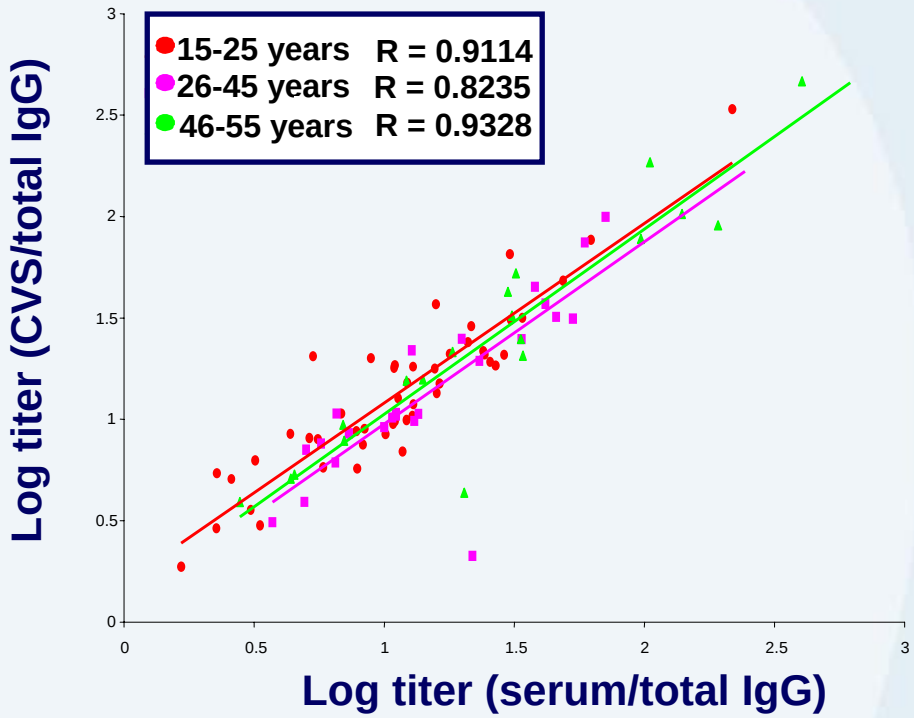


HPV-014: Correlation Between Serum and Cervico-vaginal Antibody Levels

HPV-16



HPV-18



Excellent correlation between serum and cervico-vaginal antibody levels in women ages 15 to 55 years

Analysis at 24 months post first vaccination

Presentation by T. Schwarz – Eurogin 2007
M. Stanley, D. R. Lowy, I. Frazer, Vaccine 24 Suppl 3, S106 (2006)
S. L. Giannini et al., Vaccine 24, 5937 (2006)

Safety in Women Over 25 Years*

- Pattern of solicited symptoms similar to younger women
  - Higher rates of injection site symptoms than control group but most AEs of low grade intensity
- No difference between HPV vaccine and control group in compliance with completion of 3 doses series
- Other safety endpoints:

Event type	Vaccine (N=1003)		Placebo (984)	
	n	%	n	%
Any unsolicited symptom	377	37.6	377	38.3
New onset of chronic diseases	10	1.0	10	1.0
Medically significant events[1]	135	13.5	141	14.3
Serious adverse events	29	0.9	26	0.9

[1]Events prompting physician/emergency room visits

*From study HPV-015

Conclusions: HPV Vaccination in Women Over 25 Years

- Vaccination of adult women is an unmet medical need
  - Most women not previously infected with both vaccine types
  - Previous infection does not protect against re-infection
- GSK HPV candidate vaccine is well tolerated, highly immunogenic and expected to protect women over 25 years of age
  - 100% seroconversion to both HPV-16/18 in all women
  - HPV-16 and 18 GMTs elicited in a range that correlates with protection in HPV-001/007
- Confirmatory efficacy data available in near future