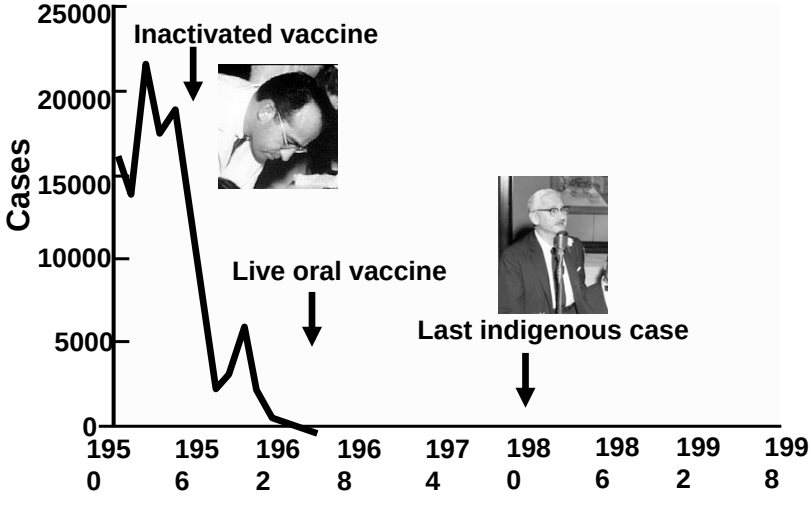
HPV Vaccines: A New Approach to Prevention of HPV Related Disease

Satellite Conference and Live Webcast

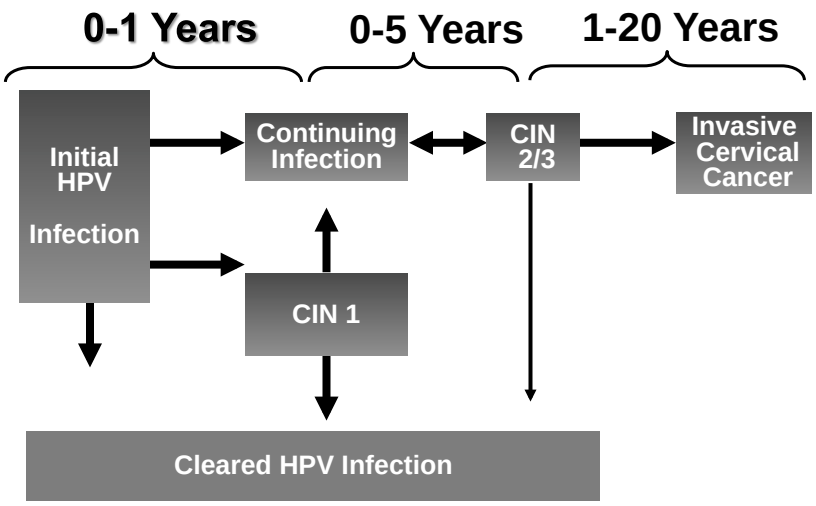
Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division

Poliomyelitis U.S., 1950 - 2002

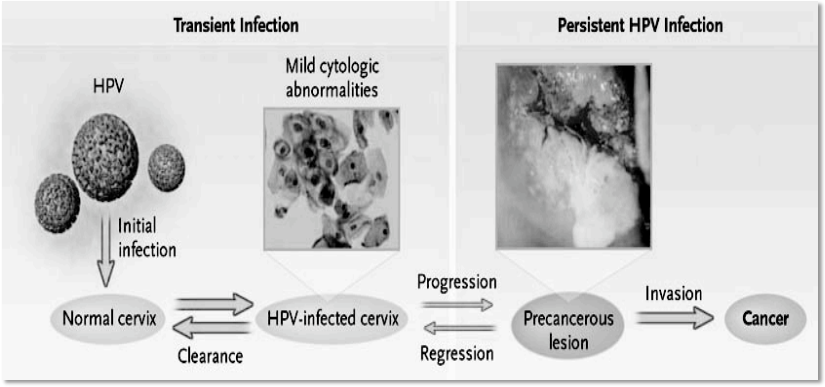


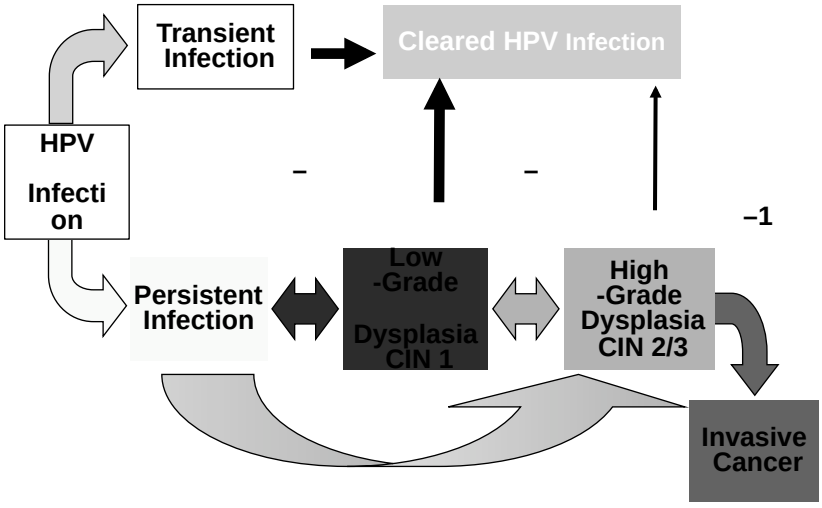
Cancers Caused By Infectious Agents Worldwide

Agent	Site	No. CA	%
H pylori	Stomach	592,000	5.5
HPV	Cervix and Others	561,200	5.2
HBV, HCV	Liver	535,000	4.9
HHV-8	Kaposi's Sarcoma	54,000	0.9
Schistosoma	Bladder	9,00000	0.1
HTLV-1	Leukemia	2,700	
Liver Flukes	Liver/Gallbladder	800	
Total Infection-Related Cancers		1,900,000	18
Total Cancers (for 2002)		10,673,000	

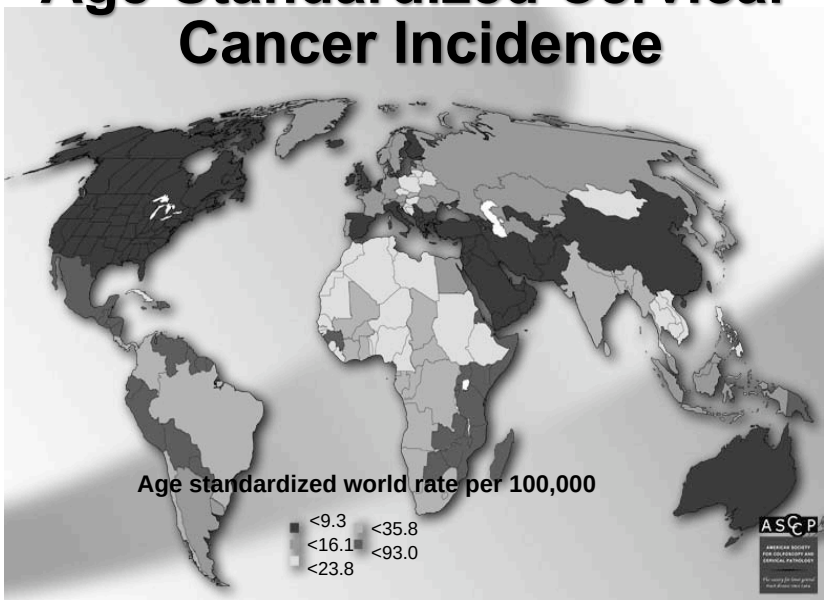


Natural History of HPV Infection and Potential Progression to Cervical Cancer[1]

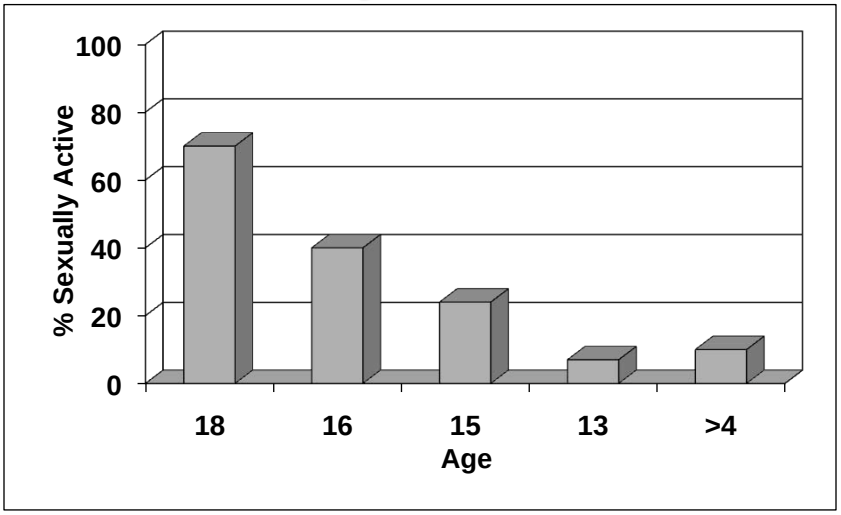




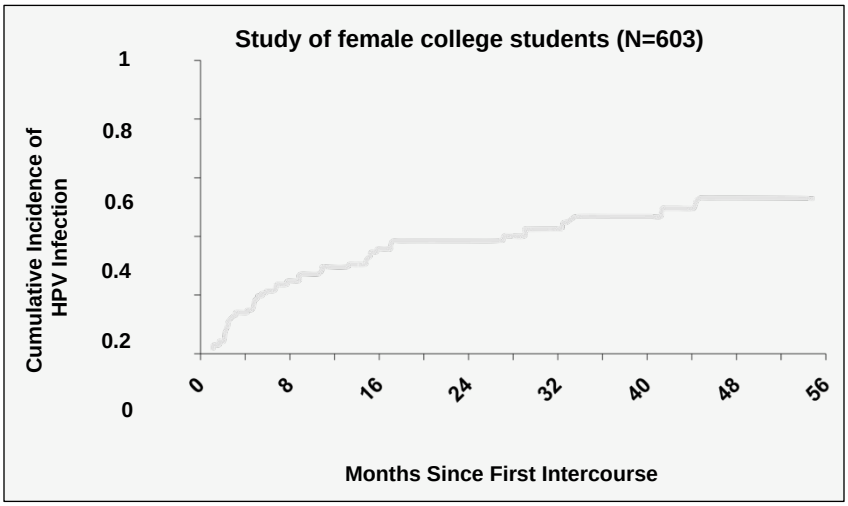
Age-Standardized Cervical Cancer Incidence

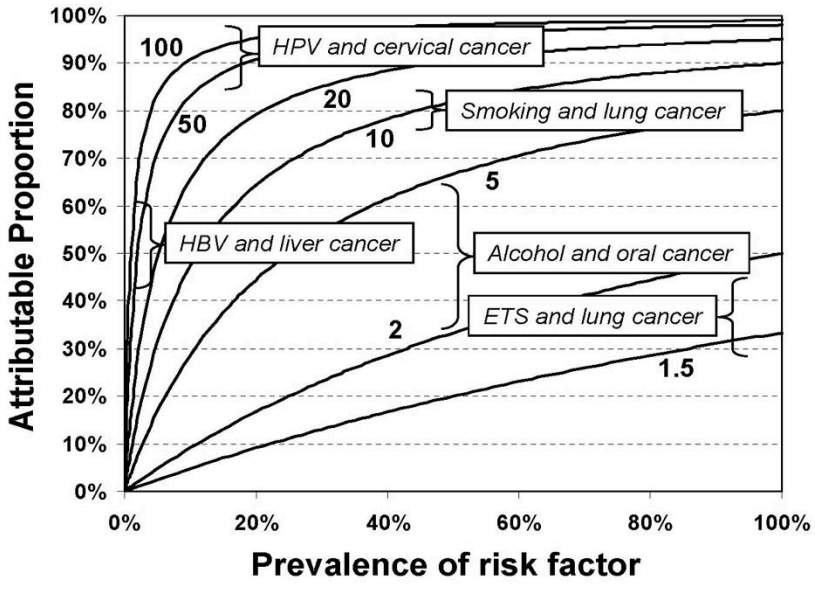


Basic U.S. Sexual Activity Statistics

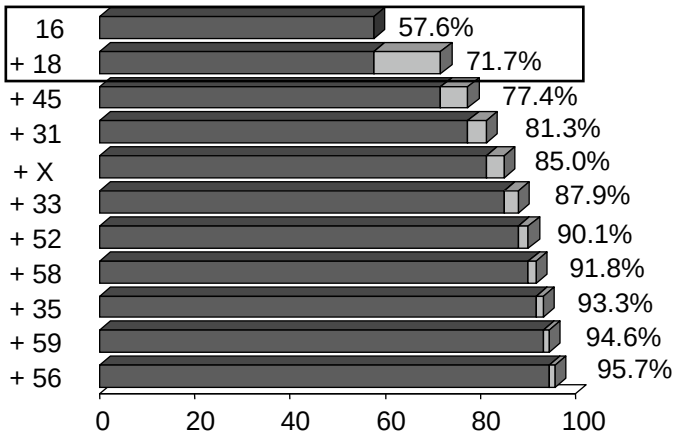


Infection From Time of First Sexual Intercourse





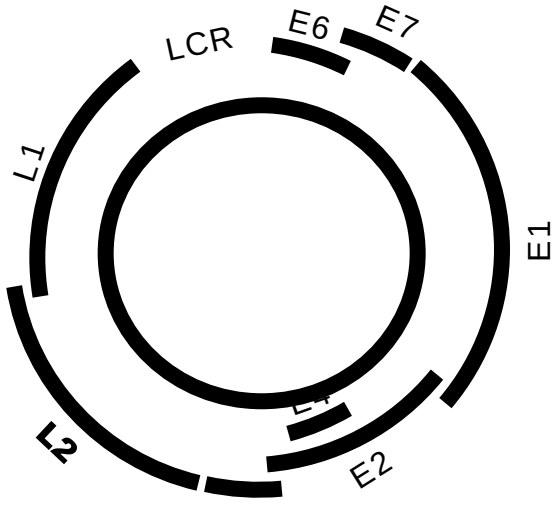
HPV Types in Cervical Cancer



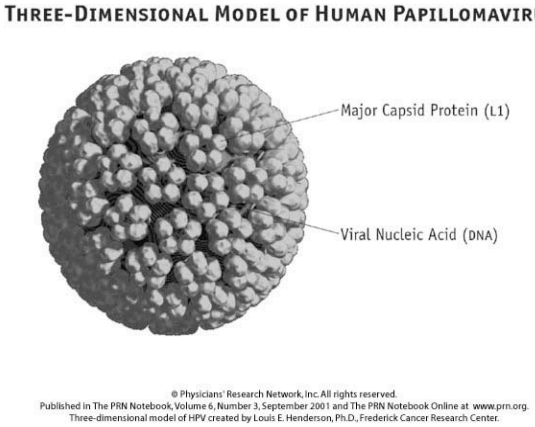
Proportion of cancers associated with HPV types

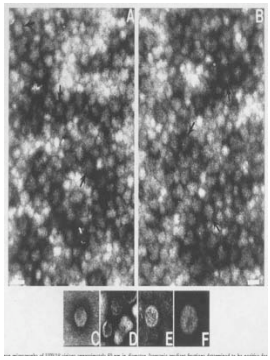
HPV 16/18 vaccine could prevent > 70% of cervical cancers

HPV Genome

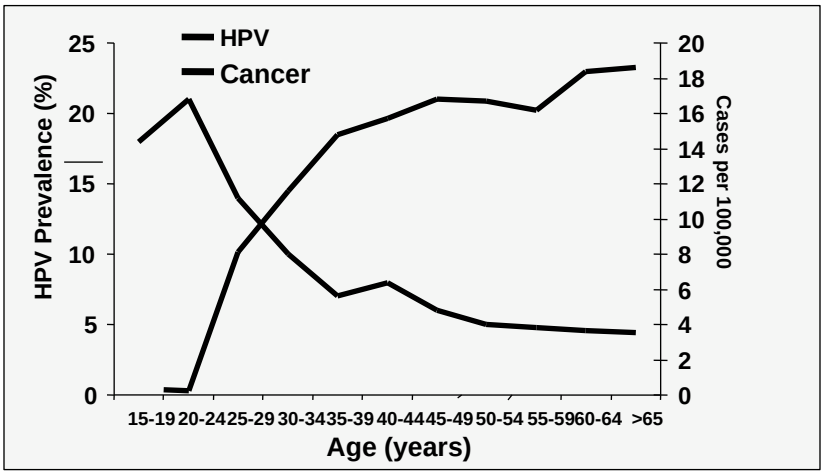


HPV Virions

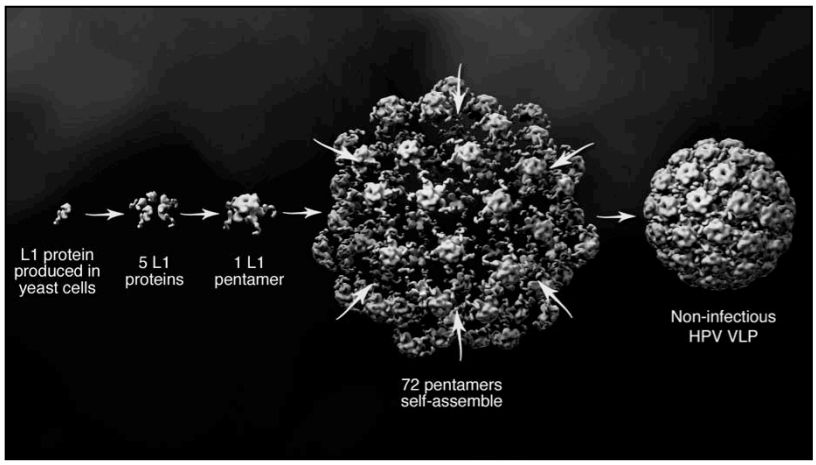


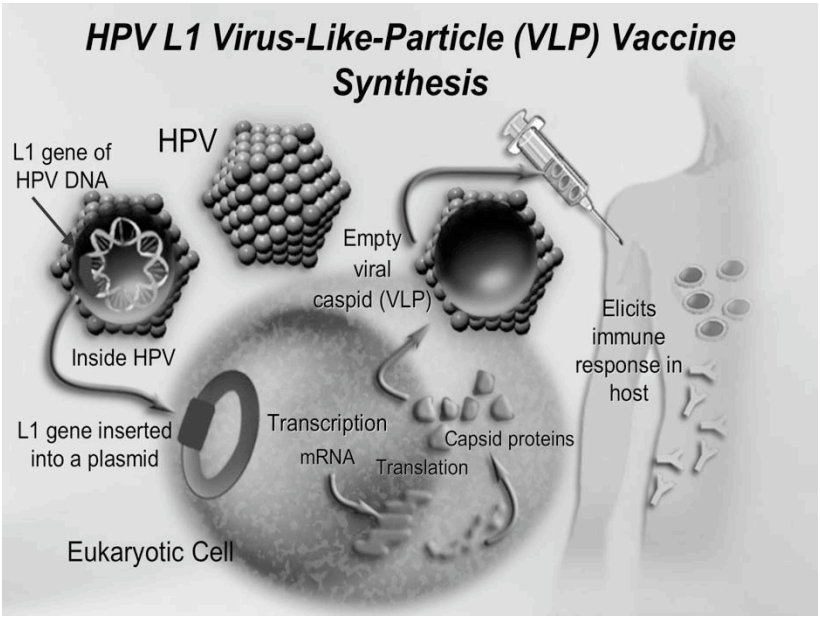


HPV Prevalence And Cervical Cancer Incidence By Age

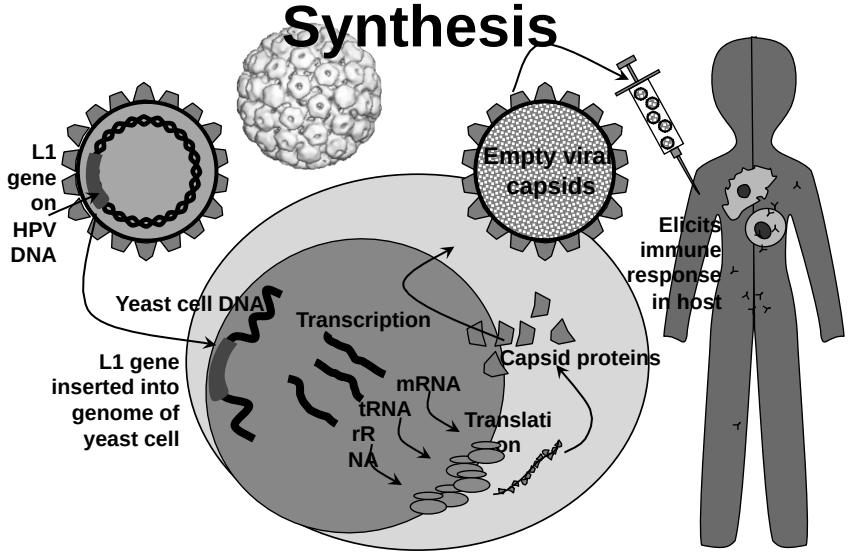


Assembly of VLPs[1–3]





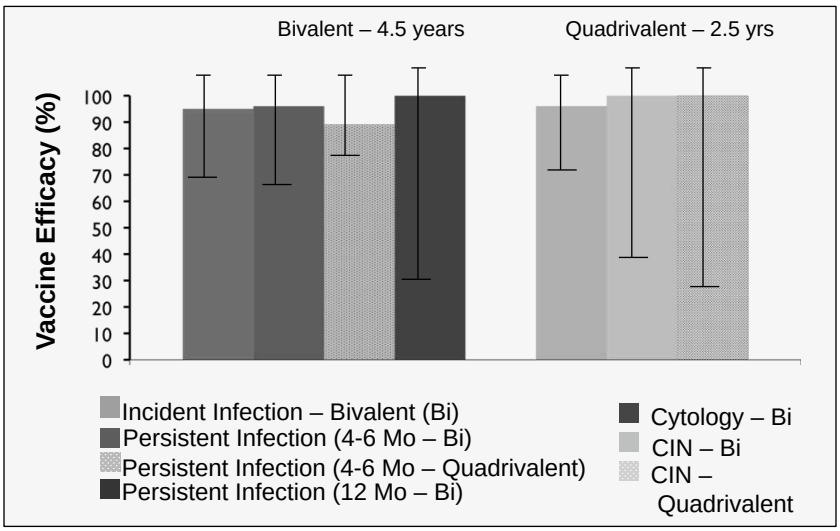
HPV L1 VLP Vaccine Synthesis



Phase II Randomized Controlled Trials

	Bivalent Vaccine	Quadrivalent Vaccine
Reference	**Harper DM et al. *Lancet.* 2004;364:1757-1765.**	**Villa LL et al. *Lancet Oncology.* 2005;6:271-278.**
Vaccine Type	Bivalent HPV-16 and HPV-18 VLP ,L1 capsid component	Quadrivalent HPV-6/11/16/18 VLP, L1 capsid component
Concentration	**HPV 6 not included** **HPV 11 not included** 20 µg HPV 16 20 µg HPV 18	**20 µg HPV 6** **40 µg HPV 11** 40 µg HPV 16 20 µg HPV 18
Adjuvant	500 µg aluminum hydroxide w/50 µg 3-deacylated monophosphoryl lipid A (AS04)	225 µg aluminum hydroxyphosphate sulfate

Efficacy for HPV 16/18 Associated Endpoints



Quadrivalent Vaccine

Phase III Trial Efficacy Results in HPV 16/18-Free Women

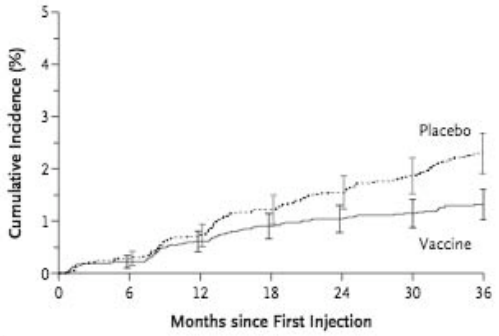
	Vaccine		Placebo		Efficacy (%)	CI	P Value
End Point	n	Cases	n	Cases			
HPV 16/18: CIN 2/3 or AIS	5,301	0	5,258	21	100	(76–100)	< 0.001
HPV 6/11/16/18: CIN 1	2,240	0	2,258	25	100	(84–100)	
HPV 6/11/16/18: Condy, VIN 1, VAIN 1	2,261	0	2,279	34	100	(89–100)	
HPV 6/11/16/18: VIN 2/3 or VAIN 2/3	2,261	0	2,279	7	100	(30-100)	

Merck - FUTURE II Study (NEJM, 2007)

	VACCINE			PLACEBO			
	Total Subjects	No. of Cases	Rate	Total Subjects	No. of Cases	Rate	Efficacy (95% CI)
Subjects in intention-to-treat population††	6087	83	0.5	6080	148	0.8	44 (26–58)
Lesion type							
Cervical intraepithelial neoplasia grade 2	6087	41	0.2	6080	96	0.5	57 (38–71)
Cervical intraepithelial neoplasia grade 3	6087	57	0.3	6080	104	0.6	45 (23–61)
Adenocarcinoma in situ	6087	5	<0.1	6080	7	<0.1	28 (<0–82)
Lesions associated with any HPV type							
Subjects in intention-to-treat population	6087	219	1.3	6080	266	1.5	17 (1–31)
Lesion type							
Cervical intraepithelial neoplasia grade 2	6087	149	0.9	6080	192	1.1	22 (3–38)
Cervical intraepithelial neoplasia grade 3	6087	127	0.7	6080	161	0.9	21 (<0–38)
Adenocarcinoma in situ	6087	5	<0.1	6080	8	<0.1	37 (<0–84)

Merck - FUTURE II Study (NEJM, 2007)

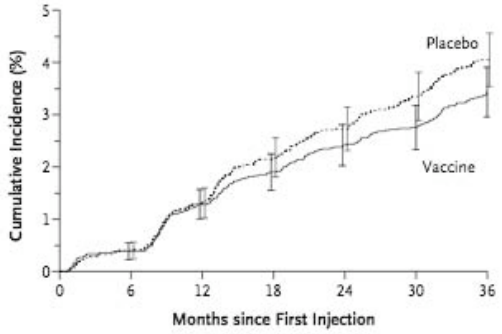
A



No. at Risk							
Vaccine	6087	5918	5824	5733	5592	5427	2925
Placebo	6080	5942	5832	5736	5586	5420	2994
Cumulative No. of Subjects with an End Point							
Vaccine	0	13	36	53	61	67	76
Placebo	0	17	43	72	91	109	132

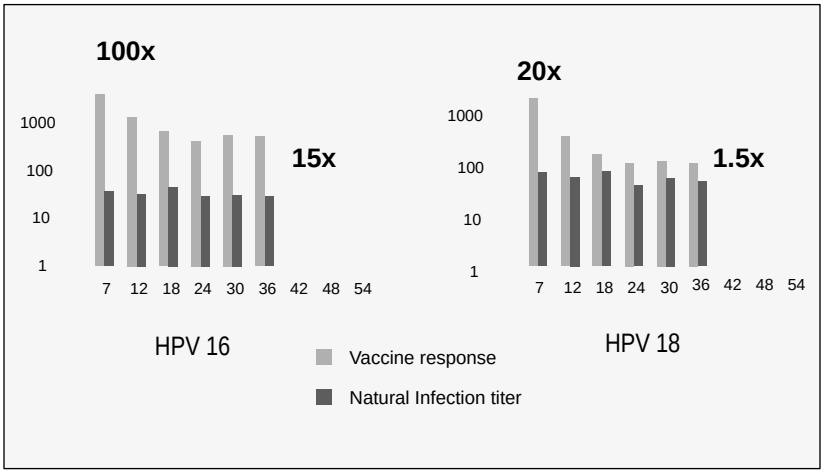
Merck - FUTURE II Study (NEJM, 2007)

B



No. at Risk							
Vaccine	6087	5915	5808	5709	5564	5406	2909
Placebo	6080	5939	5819	5718	5569	5399	2982
Cumulative No. of Subjects with an End Point							
Vaccine	0	23	76	112	142	161	196
Placebo	0	24	78	129	161	196	234

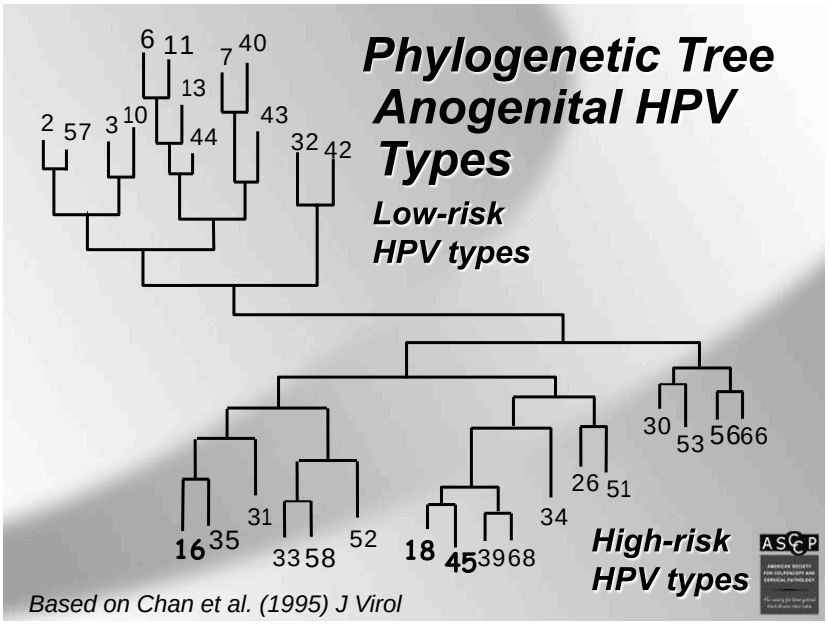
Immunogenicity Over Time (Months)



Bivalent Vaccine Protection Against Incident Phylogenetically Related HPV Infections

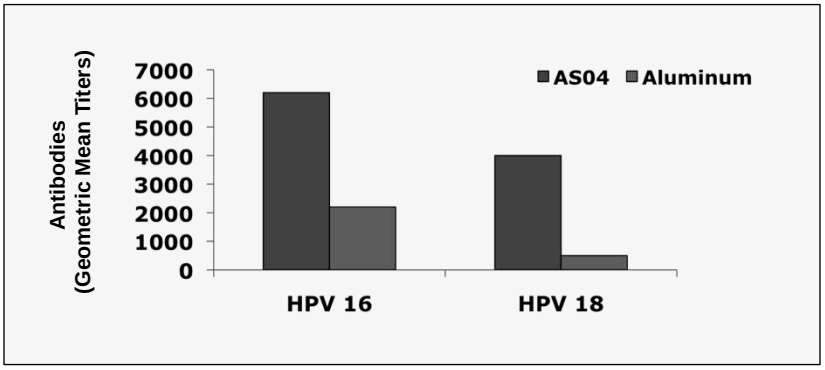
	Vaccine			Placebo			
	Total Women	Women w/ Previous HPV Event*	Event Rate (95% CI)	Total Women	Women w/ Previous HPV Event*	Event Rate (95% CI)	Vaccine Efficacy (95% CI)
HPV 45	528	1	0.1 (0-0.4)	518	17	1.2 (0.7-1.9)	**94 (63-100)**
HPV 31	528	14	0.9 (0.5-1.6)	516	30	2.1 (1.4-3.0)	**55 (12-78)**
HPV 33	529	12	0.8 (0.4-1.4)	519	13	0.9 (0.5-1.5)	9 (-117-62)
HPV 52	524	40	2.8 (2.0-3.8)	515	48	3.5 (2.6-4.6)	19 (-27-48)
HPV 58	529	14	0.9 (0.5-1.6)	517	16	1.1 (0.6-1.8)	14 (-88-61)

*Previous HPV event included any self-reported HPV 45, 31, 33, 52, or 58 event.



Role of HPV Vaccine Adjuvants

Antibody Levels at Day 210 after Vaccination with Vaccine + AS04 vs. Same Vaccine with Aluminum Salt Only



Safety of HPV Vaccines

	Bivalent Vaccine[1]	Quadrivalent Vaccine[2]
Injection Site Pain, Erythema, Edema, Fever	Yes	Yes
Acceptable Rate of Adverse Events	Yes	Yes
New Onset of Chronic Diseases after 4.5 Years	No	–
Serious Adverse Events	No	No

Vaccine-Related Experiences

Injection Site (1 to 5 Days Post-Vaccination)			
	GARDISIL (N=5,088)	Placebo (Aluminum) (N=3,470)	Placebo (Saline) (N=320)
Pain	83.9%	75.4%	48.6%
Swelling	25.4%	15.8%	7.3%
Erythema	24.6%	18.4%	12.1%
Pruritus	3.1%	2.8%	0.6%

Systemic Adverse Event(1 to 15 Days Post-Vaccination)		
	GARDISIL (N=5,088)	Placebo (N=3,790)
Fever	10.3%	8.64%

- Few subjects (0.1%) discontinued due to adverse experiences

The vaccine-related adverse experiences that were observed among recipients of GARDASIL were at a frequency of at least 1.0% and also at a greater frequency than that observed among placebo recipients

All-Cause Common Systemic Adverse Experiences*

Adverse Experience (1 to 15 Days Post-Vaccination)	GARDISIL® (N = 5,088) %	Placebo (N = 3,790) %	Adverse Experience (1 to 15 Days Post-Vaccination)	GARDISIL® (N = 5,088) %	Placebo (N = 3,790) %
Pyrexia	13.0	11.2	Cough	2.0	1.5
Nausea	6.7	6.6	Toothache	1.5	1.4
Nasopharyngitis	6.4	6.4	Upper Respiratory Tract Infection	1.5	1.5
Dizziness	4.0	3.7	Malaise	1.4	1.2
Diarrhea	3.6	3.5	Arthralgia	1.2	0.9
Vomiting	2.4	1.9	Insomnia	1.2	0.9
Myalgia	2.0	2.0	Nasal Congestion	1.1	0.9

***Greater than or equal to 1% frequency and greater than or equal to the incidence in the placebo group**

Three Phase III Trials Are in Progress

Sponsor	VLP Types	Trial Sites
Merck	HPV 16, 18, 6, 11	Multisite
GSK	HPV 16, 18	Multisite
NCl	HPV 16, 18	Costa Rica

Over 40.000 young women will be followed for several yrs Virologic Endpoint: Persistent cervical HPV DNA Clinical Endpoint CIN 2 and CIN 3

Targeting a High Disease Burden With GARDASIL®

HPV Type	Approximate Disease Burden
16 and 18	• 70% pf cervical cancer, AIS, CIN 3, VIN 2/3 and VAIN 2/3 cases • 50% of CIN cases
6, 11, 16 and 18	• 35-50% of all CIN 1, VIN 1 and VAIN 1 cases • 90% of genital warts cases

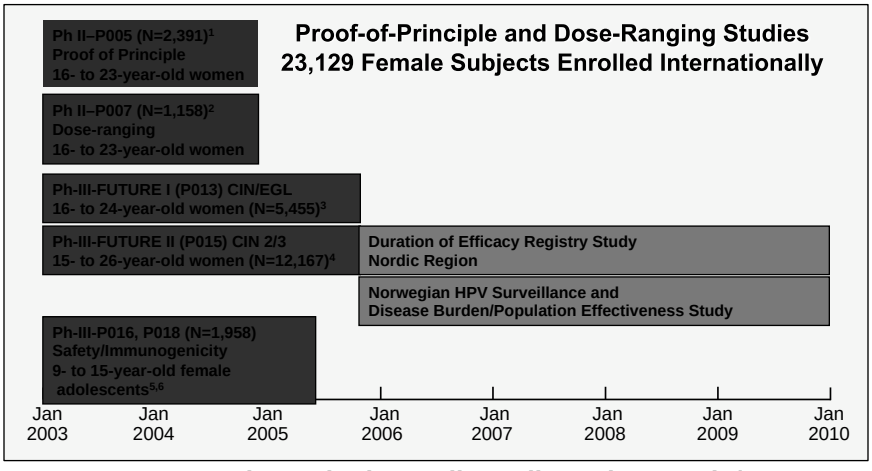
AIS = adenocarcinoma *in situ*
CIN = cervical intraepithelial neoplasia
VIN = vulvar intraepithelial neoplasia
VaIN = vaginal intraepithelial neoplasia

Clinical Program for GARDASIL®: Selection of Trial End Points[1,2]

Necessary Criteria	Possible End Points		
	HPV Infection	CIN 7	CIN 2/3 or AIS
Required Precursor for Cervical Cancer	√	—	√
Prompts Treatment	—	—	√
Reduction Leads to Cervical Cancer Reduction	—	—	√

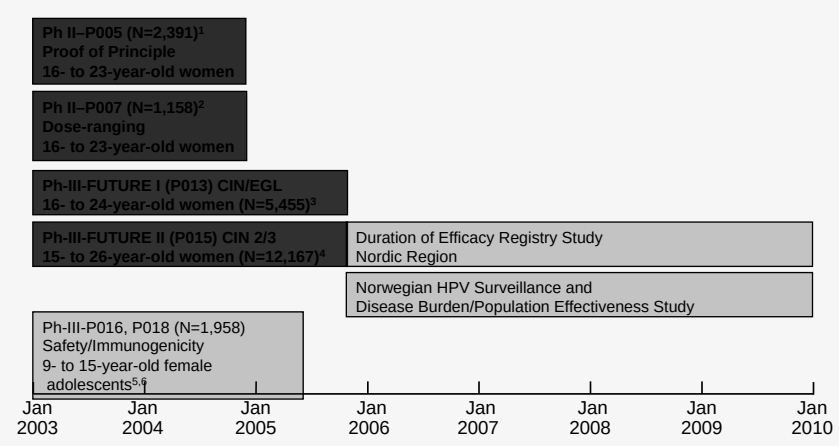
2

Phase II/III Program for GARDASIL®



FUTURE = Females United to Unilaterally Reduce Endo/ Ectocervical Disease; EGL = external genital lesions.

Clinical Program for GARDASIL® Combined Efficacy Analysis



Details of the PPE Population

	PPE Population
Sero (+) and/or PCR (+) to the relevant vaccine HPV type at Day 1	Excluded
PCR (+) to the relevant vaccine HPV type during the vaccination phase	Excluded
Protocol violators	Excluded
<3 Doses	Excluded
Case counting	1 month Postdose 3

Efficacy

100% Efficacious Against HPV 16- and 18-Related Cervical Cancer Precursors[1]

PPE-Combined Population; subjects were naïve to HPV Types 6, 11, 16, and/or 18

End Point: HPV 16/18-related	n	GARDASIL® or HPV 16 L1 VLP Cases*	n	Placebo Cases	Combined Analysis: Efficacy	Combined Analysis: 95% CI
CIN 2/3 or AIS	8,487	0	8,460	53	100%	93–100
CIN 3 or AIS†‡	8,487	0	8,460	32	100%	88–100

- **The efficacy of GARDASIL against HPV 16-, and 18-related VIN 2/3 or ValN 2/3 was 100%.**

*Analysis of CIN 2/3 and AIS endpoints included protocol 005.
†Defined by FIGO as Stage 0 cervical cancers; FIGO = International Federation of Gynecology and Obstetrics.
‡CIN 3 or AIS analysis was a secondary end point.
1. Data on file.

Efficacy Against HPV

6/11/16/18-Related Lesions[1]

PPE-Combined Population; subjects were naïve to HPV Types 6, 11, 16, and/or 18

End Point: HPV 6/11/16/18-related	GARDASIL® Cases	Placebo Cases	Combined Analysis: Vaccine Efficacy	Combined Analysis: 95% CI
	n=7,858	n=7,861		
CIN or AIS	4	83	95%	87–99

End Point: HPV 6/11/16/18-related	GARDASIL® Cases*	Placebo Cases*	Vaccine Efficacy	95% CI
	n=7,897	n=7,899		
Genital warts	1	91	99%	94–100

- **The efficacy of GARDASIL against HPV 6-, 11-, 16-, and 18-related VIN 1 or ValN 1 was 100%...**

1. Data on file, MSD.

Subjects Exposed to Any Vaccine HPV Type at Enrollment[1]

Efficacy Studies-Combined Population

Day 1 Composite HPV Status	Combined Analysis Total (N=18,478)
Negative to HPV 6/11/16/18	73%
By Serology	80%
By PCR Only	85%
Positive to at least 1 HPV type	27%
By Serology	20%
By PCR	15%

- **93% of subjects had one or none of the HPV vaccine types (6, 11, 16, or 18) at enrollment.**

Exclusion criteria: 6 or more sexual partners 1. Data on file, MSD.

Efficacy of GARDASIL® in MITT 2 Population[1]

Ph III–FUTURE I (P013) and FUTURE II (P015)

	Vaccine (N=8,799)			Placebo (N=8,800)				
Exposed to ≥1 Vaccine HPV Type at Day 1	n	Number of cases	Rate*	n	Number of cases	Rate*	Observed efficacy	95% CI
HPV 6, 11,16, or 18-Related CIN	2,190	4	0.1	2,184	32	0.8	87.5	(64.8, 96.8)
HPV 6, 11,16, or 18-Related Genital Warts, VIN 1–3, or VaIN 1–3	2,220	3	0.1	2,218	33	0.8	90.9%	(71.1, 98.2)

Impact of GARDASIL® Against HPV 6/11/16/18-Related CIN[1]

Seronegative/PCR-negative

End Point	GARDASIL® Cases (N=8,625)	Placebo Cases (N=8,673)
HPV 6/11/16/18-CIN or AIS	9	143

Seronegative/PCR-positive

End Point	GARDASIL Cases (N=797)	Placebo Cases (N=768)
HPV 6/11/16/18-CIN or AIS	70	91

Seropositive/PCR-negative

End Point	GARDASIL Cases (N=1242)	Placebo Cases (N=1283)
HPV 6/11/16/18-CIN or AIS	0	5

Seropositive/PCR-positive

End Point	GARDASIL Cases (N=568)	Placebo Cases (N=580)
HPV 6/11/16/18-CIN or AIS	94	94

1. Data on file, MSD.

MITT Populations Used to Evaluate GARDASIL®[1]

	MITT-2	MITT-3
Sero (-) and/or PCR (-) to the Relevant Vaccine HPV Type at Day 1	Included	Included
Sero (+) and/or PCR (+) to the Relevant Vaccine HPV Type at Day 1	Excluded	Included
PCR (+) to the Relevant Vaccine HPV Type During the Vaccination Phase	Included	Included
Day 1 (+) to non-vaccine HPV type	Included	Included
Day 1 Pap ≥ASCUS	Included	Included
Protocol Violators/< 3 doses	Included	Included
Case Counting	After Day 30	After Day 30

ASCUS = Atypical squamous cells of undetermined significance; those who had a normal Pap at baseline were considered part of a restricted cohort of MITT-3 called R-MITT-3.
1. Data on file, MSD.

Contribution of Subpopulations to Overall Incidence of CIN 2/3 or AIS[1]

Naïve to relevant vaccine HPV types at Day 1 (MITT-2)

- May acquire new infection prior to completion of vaccination regimen
- Takes time for disease to develop

Early on, few disease cases observed

Prophylactic efficacy of GARDASIL is high

MITT-2 + those infected with ≥1 vaccine HPV type or non-vaccine type at Day 1 (MITT-3)

- May have disease at Day 1

OR

- May develop disease after Day 1

Most disease in clinical trials of GARDASIL® was observed early

Impact of GARDASIL is masked due to early prevalence of disease

1. Data on file, MSD.

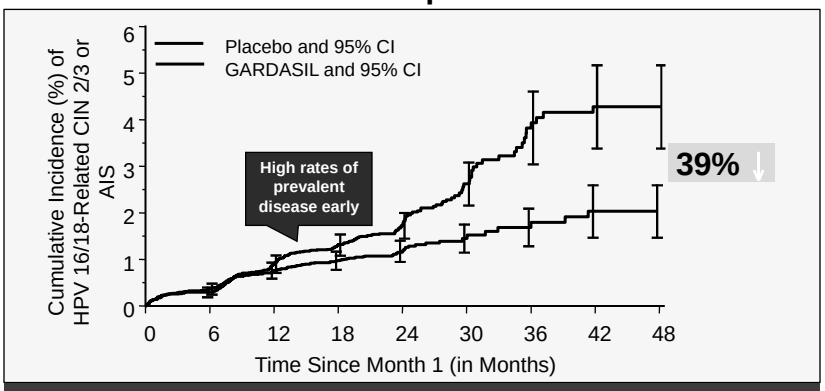
General Population Impact: In Young Women 16–26

End Points	Analysis	GARDASIL or HPV 16 Vaccine Cases	Placebo Cases	% Reduction (95% CI)
HPV 16/18-related CIN 2/3 or AIS	HPV-naïve efficacy	1	81	99 (93, 100)
	HPV 16(+) and/or 18(+) at Day 1	121	120	--
	General population impact	122	201	39 (23, 52)
HPV 6/11/16/18-related CIN or AIS	HPV-naïve efficacy	9	143	94 (88, 97)
	HPV 6, 11, 16, and/or 18 (+) at Day 1	161*	174*	--
	General population impact	170	317	46 (35, 56)
HPV 6/11/16/18-related genital warts	HPV-naïve efficacy	9	136	93 (87, 97)
	HPV 6, 11, 16, and/or 18 (+) at Day 1	49	48†	--
	General population impact	58	184	69 (58, 77)

*Includes 2 subjects who underwent colposcopy for reasons other than an abnormal Pap and 1 subject with missing serology/PCR data at Day 1.
†Includes 1 subject with missing data at Day 1.
1. Data on file, MSD.

General Population Impact: in 16- to 26-Year-Old Females Within 2 to 4 Years[1]

MITT-3 Population



With each screening round, the impact of the vaccine became more apparent.

1. Data on file, MSD.

Clinical Efficacy Studies for GARDASIL®: Study Characteristics

Study Design	Protocol 005*	Protocol 007	FUTURE I	FUTURE II
N	2,391	551	5,442	12,157
Age (years)	16 to 26			
Median duration of follow-up (years)	4.0	3.0	2.4	2.0
Vaccination schedule	Subjects received GARDASIL or placebo on the day of enrollment, and 2 and 6 months thereafter.			

FUTURE = Females United To Unilaterally Reduce Endo/Ectocervical Disease

*Protocol 005 evaluated only the HPV 16 component of GARDASIL

Clinical Program for GARDASIL®: Selection of Trial End Points[1]

Necessary Criteria	End Points		
	HPV Infection	CIN 1	CIN 2/3
Immediate precursor for cervical cancer	√	—	√
Prompts secondary prevention measures	—	—	√
Detection and removal have been shown to prevent cancer	—	—	√

Populations Used to Evaluate GARDASIL®

	PPE Population	General Population Impact
Sero (+) and/or PCR (+) to the Relevant Vaccine HPV Type at Day 1	Excluded	Included
PCR (+) to the Relevant Vaccine HPV Type During the Vaccination Phase	Excluded	Included
Protocol Violators	Excluded	Included
<3 Doses	Excluded	Included
Case Counting	1 Month Postdose 3	1 Month Postdose 1

PPE = Per-protocol efficacy

Prophylactic Efficacy

GARDASIL® Was 100% Efficacious Against HPV 16- and 18-related CIN 2/3 or AIS

Population	n	GARDASIL Cases	n	Placebo Cases	Efficacy	95% CI
Protocol 005*	755	0	750	12	100%	65.1–100
Protocol 007	231	0	230	1	100%	73.9–100
FUTURE I	2,200	0	2,222	19	100%	78.5–100
FUTURE II	5,301	0	5,258	21	100%†	80.9–100
Combined protocols	**8,487**	**0**	**8,460**	**53**	**100%†**	**92.9–100**

*Evaluated only the HPV 16 L1 VLP component of GARDASIL.
†P-values were computed for the prespecified primary hypothesis tests. All p-values were <0.001, supporting the following conclusions: efficacy against HPV 16/18-related CIN 2/3 is >0% (FUTURE II); and efficacy against HPV 16/18-related CIN 2/3 is >25% (combined protocols).

Prophylactic Efficacy

GARDASIL® Was Efficacious Against HPV 6-, 11-, 16-, and 18-related CIN (CIN 1, CIN 2/3) or AIS

Population	n	GARDASIL Cases	n	Placebo Cases	Efficacy	95% CI
Protocol 007	235	0	233	3	100%	73.8-100
FUTURE I	2,240	0	2,258	37	100%*	89.5–100
FUTURE II	5,383	4	5,370	43	90.7%	74.4–97.6
Combined protocols	**7,858**	**4**	**7,861**	**83**	**95.2%**	**87.2–98.7**

*P-values were computed for the prespecified primary hypothesis tests. All p-values were <0.001, supporting the following conclusions: efficacy against HPV 6/11/16/18-related CIN is >20% (FUTURE I).

Prophylactic Efficacy

GARDASIL® Was Efficacious Against HPV 6-, 11-, 16-, and 18-related Genital Warts

Population	n	GARDASIL Cases	n	Placebo Cases	Efficacy	95% CI
Protocol 007	235	0	233	3	100%	93.5-100
FUTURE I	2,261	0	2,279	29	100%	86.4–100
FUTURE II	5,401	1	5,387	59	98.3%	90.2–100
Combined protocols	**7,897**	**1**	**7,899**	**91**	**98.9%**	**93.7–100**

- **The efficacy of GARDASIL against HPV 6-, 11-, 16-, and 18-related VIN 1 or VaIN 1 was 100%.**

Populations Used to Evaluate GARDASIL®

	PPE Population	General Population Impact
Sero (+) and/or PCR (+) to the Relevant Vaccine HPV Type at Day 1	Excluded	Included
PCR (+) to the Relevant Vaccine HPV Type During the Vaccination Phase	Excluded	Included
Protocol Violators	Excluded	Included
<3 Doses	Excluded	Included
Case Counting	1 Month Postdose 3	1 Month Postdose 1

PPE = Per-protocol efficacy

General Population Impact

GARDASIL® Reduced HPV 16- and 18-related CIN 2/3 or AIS

HPV 16- or 18-related CIN 2/3 or AIS	N	GARDASIL or HPV 16 L1 VLP Cases	N	Placebo Cases	% Reduction	95% CI
Prophylactic Efficacy*	9,342	1	9,400	81	98.8%	93–100
HPV 16 and/or HPV 18 Positive at Day 1	--	121	--	120	--	--
General Population Impact†	9,831	122	9,896	201	39.0%	23–52

*Includes all subjects who received at least 1 vaccination and who were naïve (PCR (-) and sero (-)) to HPV 6, 11, 16, and /or 18 at Day 1.
Case counting started at 1 Month Postdose 1.
†Includes all subjects who received at least 1 vaccination (regardless of baseline HPV status at Day 1). Case counting started at 1 Month Postdose 1.

Note: Table does not include disease due to nonvaccine HPV types.

General Population Impact

GARDASIL® Reduced HPV 16- and 18-related VIN 2/3 or VaIN 2/3

HPV 16- or 18-related VIN 2/3 and VaIN 2/3	N	GARDASIL or HPV 16 L1 VLP Cases	N	Placebo Cases	% Reduction	95% CI
Prophylactic Efficacy*	8,641	0	8,667	24	100%	83–100
HPV 16 and/or HPV 18 Positive at Day 1	--	8	--	2	--	--
General Population Impact†	8,954	8	8,962	26	69.1%	30–88

*Includes all subjects who received at least 1 vaccination and who were naïve (PCR (-) and sero (-)) to HPV 6, 11, 16, and /or 18 at Day 1.
Case counting started at 1 month Postdose 1.
**Includes all subjects who received at least 1 vaccination (regardless of baseline HPV status at Day 1). Case counting started at 1 month Postdose 1.

Note: Table does not include disease due to nonvaccine HPV types.

General Population Impact

GARDASIL® Reduced HPV 6-, 11-, 16- and 18-related CIN or AIS

HPV 6-, 11-, 16-, 18-related CIN (CIN 1, CIN 2/3) or AIS	N	GARDASIL or HPV 16 L1 VLP Cases	N	Placebo Cases	% Reduction	95% CI
Prophylactic Efficacy*	8,625	9	8,673	143	93.7%	88–97
HPV 6, 11, 16 and/or HPV 18 Positive at Day 1	--	161†	--	174†	--	--
General Population Impact‡	8,814	170	8,846	317	46.4%	35–56

*Includes all subjects who received at least 1 vaccination and who were naïve (PCR (-) and sero (-)) to HPV 6, 11, 16, and /or 18 at Day 1.
Case counting started at 1 month Postdose 1.
†Includes 2 subjects (1 in each vaccination group) who underwent colposcopy for reasons other than an abnormal Pap and 1 placebo subject with missing serology/PCR data at Day 1.
‡Includes all subjects who received at least 1 vaccination (regardless of baseline HPV status at Day 1). Case counting started at 1 month Postdose 1.

Note: Table does not include disease due to nonvaccine HPV types.

General Population Impact

GARDASIL® Reduced HPV 6-, 11-, 16- and 18-related Genital Warts

HPV 6-, 11-, 16-,18-related Genital Warts	N	GARDASIL or HPV 16 L1 VLP Cases	N	Placebo Cases	% Reduction	95% CI
Prophylactic Efficacy*	8,760	9	8,786	136	93.4%	87–97
HPV 6, 11, 16 and/or HPV 18 Positive at Day 1	--	49	--	48†	--	--
General Population Impact‡	8,954	58	8,962	184	68.5%	57–77

*Includes all subjects who received at least 1 vaccination and who were naïve (PCR (-) and sero (-)) to HPV 6, 11, 16, and /or 18 at Day 1.
Case counting started at 1 month Postdose 1.
†Includes 1 subject with missing serology/PCR data at Day 1.
‡Includes all subjects who received at least 1 vaccination (regardless of baseline HPV status at Day 1). Case counting started at 1 month Postdose 1.

Note: Table does not include disease due to nonvaccine HPV types.

Immune Response to GARDASIL®: PPI Population

*Number of subjects randomized to the respective vaccination group who received at least 1 injection

**Number of subjects in the per-protocol analysis with data at the specified study time point

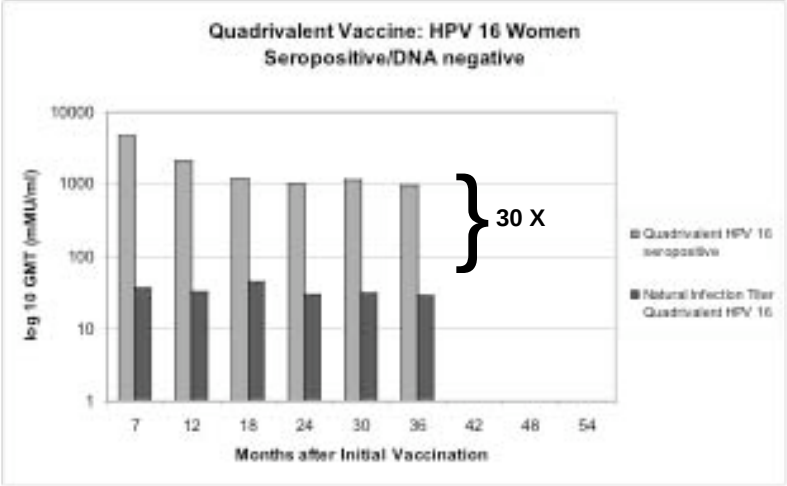
†mMU = milli-Merck units

Note: These data are from Protocol 007

Study Time	GARDASIL (N* = 276)		Aluminum-Containing Placebo (N = 275)	
	n**	GMT (95% CI) mMU/mL†	n	GMT (95% CI) mMU/mL
Anti-HPV 6				
Month 07	208	582.2 (527.2, 642.8)	198	4.6 (4.3, 4.8)
Month 24	192	93.7 (82.2, 106.9)	188	4.6 (4.3, 5.0)
Month 36	183	93.8 (81.0,108.6)	184	5.1 (4.7, 5.6)
Anti-HPV 11				
Month 07	208	696.5 (617.8, 785.2)	198	4.1 (4.0, 4.2)
Month 24	190	97.1 (84.2, 112.0)	188	4.2 (4.0, 4.3)
Month 36	174	91.7 (78.3, 107.3)	180	4.4 (4.1, 4.7)
Anti-HPV 16				
Month 07	193	3889.0 (3318.7, 4557.4)	185	6.5 (6.2, 6.9)
Month 24	174	393.0 (335.7, 460.1)	175	6.8 (6.3, 7.4)
Month 36	176	507.3 (434.6, 592.0)	170	7.7 (6.8, 8.8)
Anti-HPV 18				
Month 07	219	801.2 (693.8, 925.4)	209	4.6 (4.3, 5.0)
Month 24	204	59.9 (49.7, 72.2)	199	4.6 (4.3, 5.0)
Month 36	196	59.7 (48.5, 73.5)	193	4.8 (4.4, 5.2)

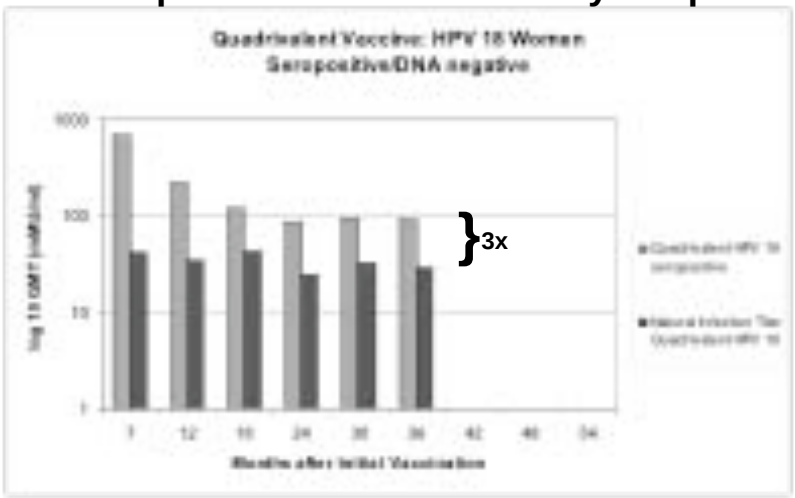
Immunogenicity of Quadrivalent Vaccine

Prior Exposure Doubles Antibody Response

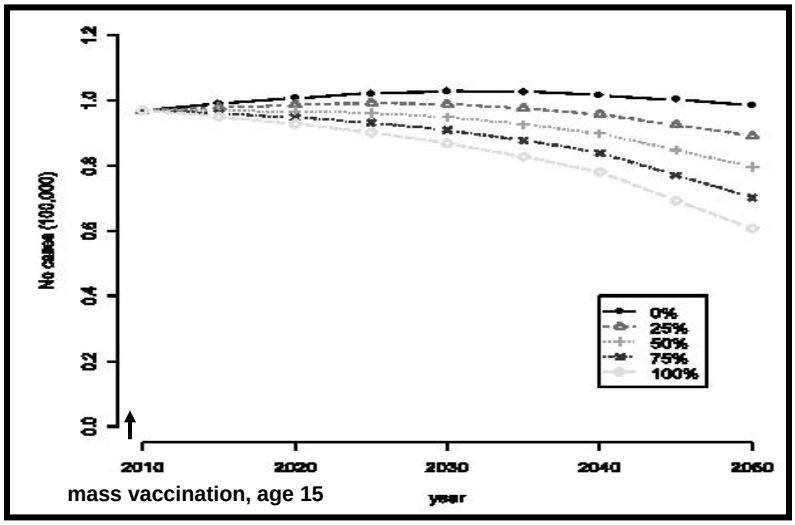


Immunogenicity of Quadrivalent Vaccine

Prior Exposure Doubles Antibody Response



HPV Vaccine for Prevention Minimal Impact in Near Future



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LIFESTYLE

[SECTION D]

Monday, February 12, 2007

HEALTH

Voluntary HPV vaccine may lessen impact

By ANNA VELASCO
News staff writer

Alabama's plan to offer the cervical cancer vaccine on a voluntary basis avoids a public outcry over forcing young girls to be inoculated against a sexually transmitted disease. But some medical experts worry that voluntary vaccination means less chance of eventually eliminating some of the worst strains of human papillomavirus.

HPV is the most common sexually transmitted disease in the country, with 20 million people infected and six million new cases annually.

Last year the Food and Drug Administration approved Gardasil, a Merck & Co. vaccine that protects against strains of HPV that cause 70 percent of cervical cancers and 90 percent of genital warts. The drug has been approved for use in females ages 9 -26. Clinical trials testing the safety and effectiveness of the vaccine in boys are still under way.

Gov. Rick Perry of Texas caused an uproar in his state when he issued an executive order requiring that girls entering the sixth grade be vaccinated starting in September 2008. Parents can opt out for religious, moral or medical reasons, but otherwise the vaccines are automatic.

Dr. Don Williamson, State Health Officer, announced last week that the Alabama Department of Public Health will ask the Legislature for $4 million to make the vaccine available in the fall to uninsured girls who want it but don't qualify for the federal Vaccine for Children program. Medicaid patients have access to Gardasil through the national vaccine program.

The state would target 11- and 12-year-old girls and try to vaccinate 10,000 to 20,000 annually with the extra appropriation, Williamson said. But he said it will not be mandatory.

"Rather than embark on a mandate, it makes a lot more sense at least to start with education and availability," Williamson said. "We're going to ask for the $4 million to serve as a safety net so that everyone who wants the vaccine has access to it."

Private insurance companies are covering the pricey Gardasil, which costs $360 for three doses given over six months.

Dr. Warner Huh, an OB/GYN oncologist at the University of Alabama at Birmingham, said he's concerned about the amount of money that will be spent to vaccinate a population only partially.

"Vaccinations don't work well if you selectively vaccinate pockets of the populations."

See VACCINE | Page 2D

SPECIAL

Last year the Food and Drug Administration approved Gardasil, a Merck & Co. vaccine that protects against strains of HPV that cause 70 percent of cervical cancers and 90 percent of genital warts.