

Zoster Vaccines – New Data on Effectiveness

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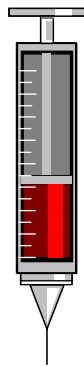
Strategies to Enhance Protection of Older Adults Against Vaccine-Preventable Diseases

- Improve Immune Response to Vaccines
 - Live, attenuated
 - Higher dose
 - Adjuvants
 - Conjugates
 - Subunit
 - DNA
 - Recombinant vector



Live Attenuated Zoster Vaccine

- Live, attenuated, cell-free preparation of Oka/Merck strain VZV
- Contains whole live virus, viral antigen and
- Neomycin, sucrose, gelatin, glutamate, inorganic salts



- Formulated to contain substantially more live virus and viral antigen than are contained in the varicella vaccine

www.cdc.gov/mmwr/preview/mmwrhtml/rr5705a1.htm

Shingles Prevention Study

- *Design:* Randomized, double-blind, placebo-controlled, stratified by age, 60-69 and ≥ 70 years
- *Setting:* 22 US sites (16 VA and 6 university medical centers)
- *Participants:* 38,546 immunocompetent adults ≥ 60 years old
 - 19,270 zoster vaccine
 - 19,276 placebo

Oxman M et al. N Engl J Med. 2005;352:2271-2284

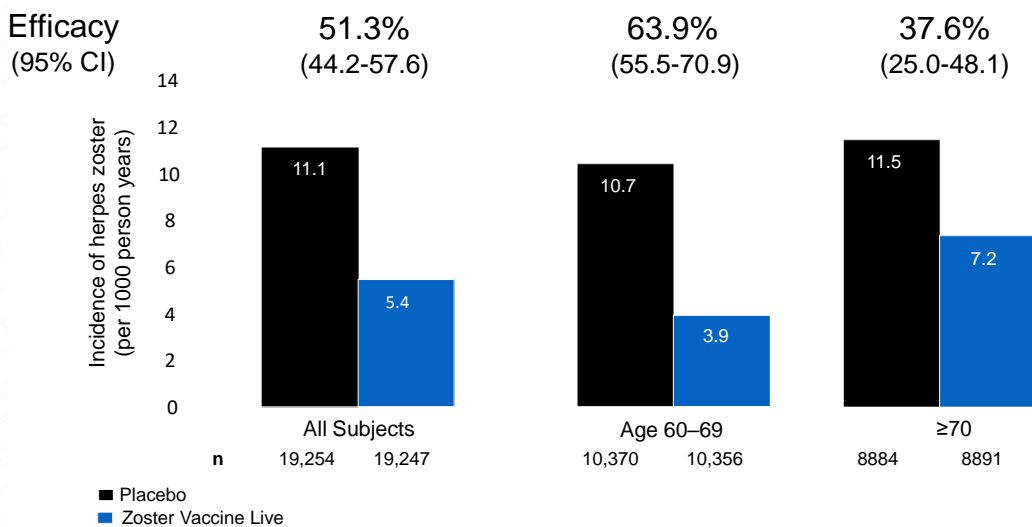
Shingles Prevention Study

- *Intervention:* One dose of live attenuated zoster vaccine or placebo
- *Outcomes:* Incidence of HZ and PHN and Pain Burden of Illness (BOI)



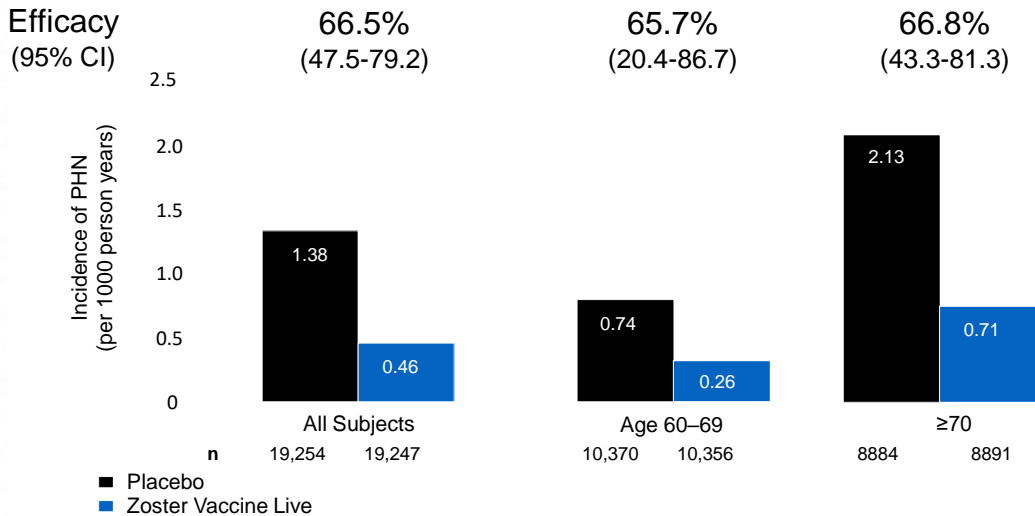
Oxman M et al. N Engl J Med. 2005;352:2271-2284

Efficacy of Live Zoster Vaccine Incidence of Herpes Zoster



Oxman MN et al. N Engl J Med. 2005;352:2271-2284

Efficacy of Live Zoster Vaccine Incidence of Postherpetic Neuralgia



Oxman MN et al. N Engl J Med. 2005;352:2271-2284

How Persistent is the Effect of the Live Zoster Vaccine?

VA CSP #403B: The Short-Term Persistence Substudy*

- Follow-up 3.3 to 7.8 years
- Comparator: Placebo
- Vaccine Efficacy for HZ: 39.6%

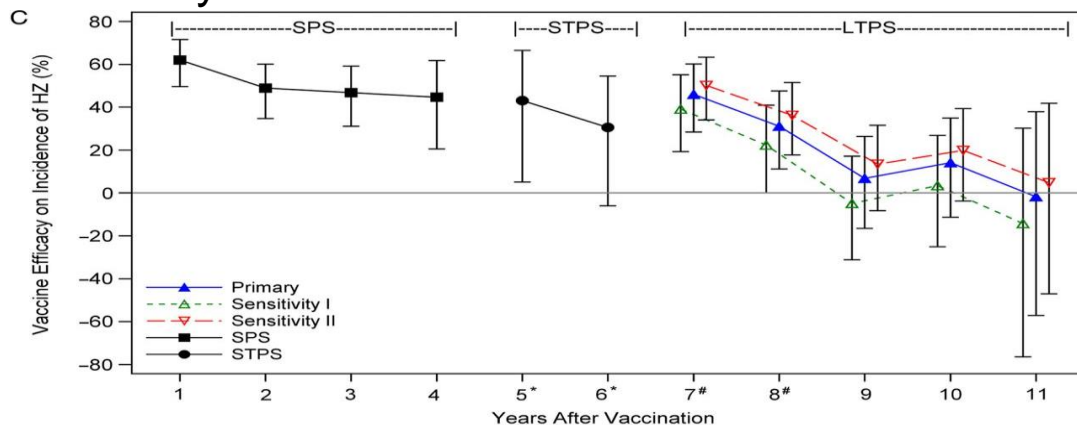
VA CSP #403C: The Long-Term Persistence Substudy**

- Follow-up 4.7 to 11.6 years
- Comparator: Historical controls
- Vaccine Efficacy for HZ: 21%

*Schmader KE et al. Clin Infect Dis 2012;55(10):1320-8

**Morrison V et al. Clin Infect Dis 2015;60:900-909

Efficacy of Live Zoster Vaccine on Herpes Zoster by Year After Vaccination



Primary										
Sensitivity I										
Sensitivity II										
SPS	62.0	48.9	46.8	44.6						
STPS					43.1	30.6				

SPS = Shingles Prevention Study; STPS = Short-Term Persistence Substudy; LTPS = Long-Term Persistence Substudy

Morrison et al. Clin Infect Dis. 2015;60:900-909; Schmader KE et al. Clin Infect Dis 2012;55:1320-8

So . . .What about a booster dose?

- Live zoster vaccine administered as a booster dose ≥ 10 years after first dose in individuals ≥ 70 years old
 - Significantly increases immunity to VZV
 - Increase in VZV immunity in the booster dose group is significantly higher than matched first-time immunization group for one year after immunization
- But clinical significance of immunological findings is unknown . . .
 - ACIP does not recommend a second dose of live zoster vaccine at this time

Levin MJ, Schmader KE, et al. J Infect Dis 2016;213:14-22

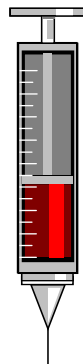
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Adjuvanted Zoster Subunit Vaccine

- Recombinant VZV glycoprotein E (gE) antigen and
- Liposome-based AS01b adjuvant
- Liposome is a spherical vesicle having at least one lipid bilayer



- AS01b adjuvant system contains:
 - monophosphoryl lipid A (MPL) and
 - saponin, a phytochemical (*Quillaja saponaria*)



Adjuvanted Zoster Subunit Vaccine Trial ZOE-50

- *Design:* Randomized, double-blind, placebo-controlled in persons ≥ 50 years old, stratified by age, 50-59, 60-69, 70-79, ≥ 80
- *Setting:* Multiple centers in North America, Europe, Latin America, Asia-Pacific
- *Participants:* 14,759 immunocompetent adults
 - 7344 zoster vaccine
 - 7415 placebo

Lal et al. New Engl J Med 2015;372:2087-2096

Adjuvanted Zoster Subunit Vaccine Trial ZOE-50

- *Intervention:* 2 doses of subunit zoster vaccine or placebo at 2 month intervals
- *Outcomes:* Incidence of HZ and PHN



Lal et al. New Engl J Med 2015;372:2087-2096

Efficacy of Adjuvanted Zoster Subunit Vaccine ZOE-50

Vaccine (n=7344)		Placebo (n=7415)		Vaccine Efficacy % (95% CI)
HZ Cases (n)	Incidence per 1000 person-yrs	HZ Cases (n)	Incidence per 1000 person-yrs	
6	0.3	210	9.1	97.2 (93.7-99.0)

Lal et al. New Engl J Med 2015;372:2087-2096

ZOE-50 Adverse Events and Reactogenicity

Reactogenicity Subgroup Within 7 Days After Vaccination

Variable	Vaccine % (95% CI)*	Placebo % (95% CI)*
Any adverse event	84.4 (83.3-85.5)	37.8 (36.4-39.3)
-Grade 3 [†] vaccination related	15.6 (14.5-16.7)	1.9 (1.5-2.3)
Injection site reaction	81.5 (80.3-82.6)	11.9 (11.0-12.9)
-Grade 3	9.5 (8.7-10.4)	0.4 (0.2-0.6)
Systemic reaction	66.1 (64.7-67.6)	29.5 (28.2-30.9)
-Grade 3	11.4 (10.5-12.4)	2.4 (2.0-2.9)

*Vaccine n = 4460, Placebo n = 4466

[†]Grade 3 – prevented normal activity

Lal et al. New Engl J Med 2015;372:2087-2096

ZOE-50 Adverse Events and Reactogenicity

Total Cohort Throughout Study Period

Variable	Vaccine % (95% CI)*	Placebo % (95% CI)*
Serious adverse event	9.0 (8.3-9.6)	8.9 (8.3-9.6)
Potential immune-mediated disease	1.0 (0.8-1.3)	1.3 (1.0-1.5)
Death	2.2 (1.9-2.5)	2.3 (1.9-2.6)

*Vaccine n = 7698, Placebo n = 7713

Lal et al. New Engl J Med 2015;372:2087-2096

Efficacy of Adjuvanted Zoster Subunit Vaccine ZOE-70

Vaccine (n=6541)		Placebo (n=6622)		Vaccine Efficacy % (95% CI)
HZ Cases (n)	Incidence per 1000 person-yrs	HZ Cases (n)	Incidence per 1000 person-yrs	
23	0.9	223	9.2	89.8 (84.2-93.7)

Cunningham AL, et al. N Engl J Med 2016;375:0191-1032

US Vaccination Coverage among Older Adults for Zoster Vaccine, 2015

Vaccine	Coverage (%)
Zoster, ever	31

National Health Interview Survey, United States, 2015
<https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/coverage-estimates/2015.html#table5>

ZOE-70 Adverse Events and Reactogenicity Reactogenicity Subgroup Within 7 Days After Vaccination

Variable	Vaccine % (95% CI)*	Placebo % (95% CI)*
Any adverse event	79.0 (75.2-82.5)	29.5 (25.6-33.7)
-Grade 3 [†]	11.9 (9.2-15.0)	2.0 (1.0-3.6)
Injection site reaction, pain	74.1 (70.0-77.8)	9.9 (7.4-12.8)
-Grade 3	8.5 (6.2-11.3)	0.2 (0.0-1.1)
Systemic reaction	53.0 (48.5-57.4)	25.1 (21.4-29.2)
-Grade 3	6.0 (4.1-8.4)	2.0 (1.0-3.6)

*Vaccine n = 505, Placebo n = 505

Cunningham AL, et al. N Engl J Med 2016;375:0191-1032

[†]Grade 3 – prevented normal activity

ZOE-70 Adverse Events and Reactogenicity

Total Cohort Throughout Study Period

Variable	Vaccine % (95% CI)*	Placebo % (95% CI)*
Serious adverse event	16.6 (15.7-17.5)	17.5 (16.6-18.4)
Potential immune-mediated disease	1.3 (1.1-1.6)	1.4 (1.1-1.7)
Death	6.1 (5.6-6.7)	6.6 (6.0-7.2)

*Vaccine n = 6950, Placebo n = 6950 Cunningham AL, et al. N Engl J Med 2016;375:0191-1032