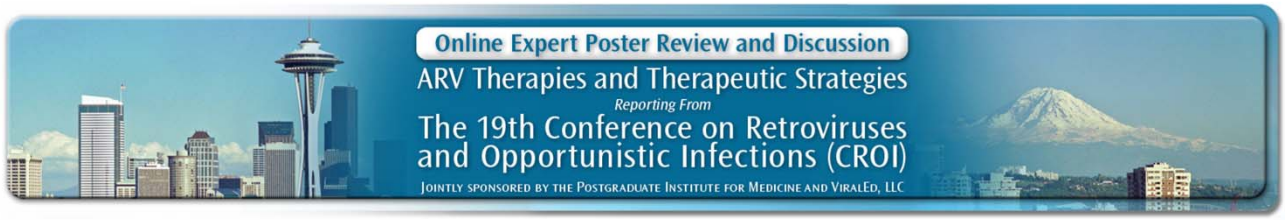

Zostavax® is Generally Safe and Immunogenic in HIV-Infected Adults with CD4 Counts ≥200 Cells/µL Virologically Suppressed on ART: Results of a Phase 2, Randomized, Placebo-Controlled Trial

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for the ACTG A5247 Team

Abstract #96

Background and Rationale

- Incidence/severity of herpes zoster (HZ) and post-herpetic neuralgia (PHN) is increased in HIV-infected patients, particularly in those with immunosuppression or immune reconstitution inflammatory syndrome
- Early antiviral therapy (e.g. acyclovir) may not abort HZ or prevent PHN and is less effective in those with advanced immunosuppression
- Zoster vaccine (Zostavax® [ZV]; Merck) reduced incidence and severity of HZ (by 51.3% and 61.1%, respectively) and PHN (by 66%) in healthy adults ≥60 years of age

Oxman MN, et al. NEJM 2005; 352:2271-8

A5247 Study Hypotheses

- **Primary:** Two doses of ZV will be generally well tolerated in HIV-infected adults with conserved immune function (CD4 T cell count ≥200 cells/µL) who are virologically suppressed on antiretroviral therapy (ART)
- **Secondary:** The geometric mean titer (GMT) of varicella zoster virus (VZV) antibody, as measured by glycoprotein enzyme-linked immunosorbent assay (gpELISA), 6 weeks post vaccination will be higher in ZV recipients than in placebo recipients

Benson CA, et al. 19th CROI; Seattle, WA; March 5-8, 2012; Abst. 96.

A5247 Study Design

- Multicenter (43 sites), double-blind, randomized (3:1), placebo-controlled safety, tolerability and immunogenicity study (N=395) of 2 doses of ZV administered on day) and at week 6
- **Inclusion Criteria:**
  - HIV-infected person age ≥18 years on stable ART; undetectable plasma HIV RNA; CD4 ≥200 cells/µL
  - Hemoglobin ≥7.0 gm/dL; platelet count ≥ 50,000/µL; creatinine ≤3 x ULN; AST, ALT and alkaline phosphatase ≤5 x ULN
  - History of varicella or HZ >1 year prior to entry or VZV seropositive at any time prior to entry

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A5247 Primary Safety Results

	ZV (N=295) N (Estimate % [95% CI])	Placebo (N=97) N (Estimate % [95% CI])	*P*-Value**
Primary Safety Endpoints	15 5.1% [2.9, 8.2]*	2 2.1% [0.3, 7.3]	0.261
Injection Site Reactions	124 42.0% [36.3, 47.9]	12 12.4% [6.6, 20.6]	<0.001
Rash	15 5.1% [2.9, 8.2]	4 4.1% [1.1, 10.2]	1.00
Fever	12 4.1% [2.1, 7.0]	6 6.2% [2.3, 13.0]	0.405

*Based on exact permutation, adj. for 2-stage design;
** Fisher's exact test

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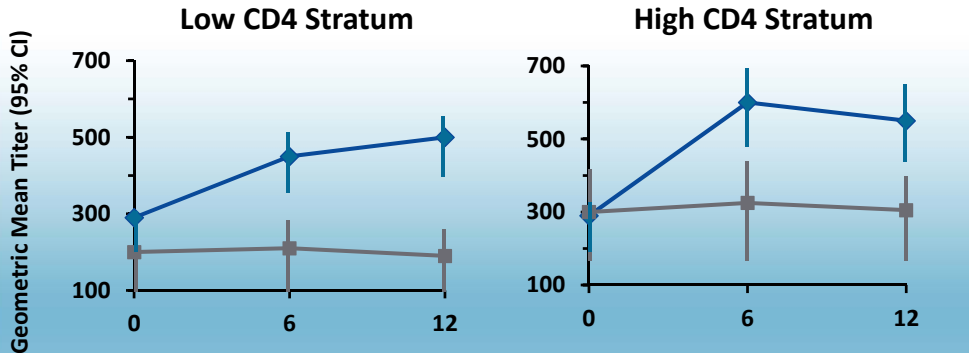
VZV gpELISA Titers by CD4 Stratum



	Low CD4 Stratum			High CD4 Stratum		
n	140	134	130	149	150	143
GMT	288.4	473.9	506.8	296.8	594.9	552.6
95% CI	(245.7, 338.6)	(407.1, 551.6)	(437.6, 586.9)	(248.6, 354.5)	(511.7, 691.7)	(476.1, 641.4)
n	47	46	43	50	50	47
GMT	203.1	213.9	198.5	304.2	319.6	309.5
95% CI	(142.5, 289.6)	(147.6, 310.0)	(135.8, 290.0)	(210.9, 438.9)	(223.1, 457.8)	(212.1, 451.5)

Benson CA, et al. 19th CROI; Seattle, WA; March 5-8, 2012; Abst. 96.