CD4 Counts Shape Humoral Responses to the Recombinant Zoster Vaccine in People With HIV

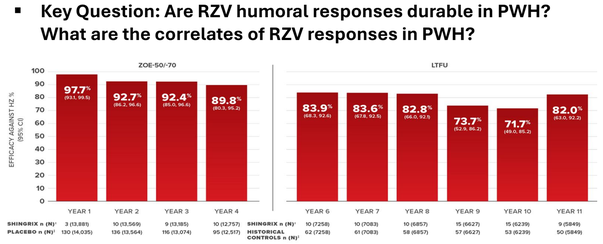
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Poster # C-06

Background

- The adjuvanted subunit recombinant zoster vaccine (RZV) was licensed in 2017 for adults ≥50 yrs, as a two-dose series
- Licensing studies (ZOE-50 and ZOE-70) suggest 97% efficacy in those ≥50 yrs and 90% efficacy in those ≥70 yrs
- In 2021, ACIP recommended a similar schedule for immunocompromised adults ≥19 years
- **Routine boosters are not recommended**
- Extended follow up of participants from the licensing studies suggest ~80% cumulative efficacy 6 to 11 years post vaccine receipt
- Humoral and cell mediated immune responses following a 2-dose series resulted in >5-fold above baseline at 10 yrs
- Mathematical models predict immunity for ≥15–20 yrs
- **Key Question: Are RZV humoral responses durable in PWH? What are the correlates of RZV responses in PWH?**



Vaccine Efficacy | SHINGRIX (Zoster Vaccine Recombinant, Adjuvanted)

Methods

Study Population

- The U.S. Military HIV Natural History Study (NHS) is a longitudinal cohort of PWH >18 years of age and eligible for care in the Department of War (DoW). Study visits occur about once every 6-12 months. Trained personnel collect ART history and results of laboratory testing including viral load and CD4 counts
- The NHS is a racially diverse, early diagnosed and treated cohort with access to care and a robust repository of serum and PBMC samples

Inclusion Criteria

- NHS participants who had received 2 doses of RZV (≥ 2 months apart)
- Availability of paired serum samples pre vaccination (3 years prior) and at two time points post vaccination (the first within 12 months and the second 3 to 5 years post dose 2 of the vaccine)

Humoral Responses

- Antibodies (Ab) against varicella glycoprotein (gE) concentrations were measured using a quantitative enzyme-linked immunosorbent assay
- Ab levels are reported as geometric mean concentrations (GMC) with 95% confidence intervals (CI), and fold changes as geometric mean fold rise (GMFR) and geometric mean fold declines (GMFD)

Methods (cont.)

- To assess the adequacy of the assay, control specimens from People Without HIV (PWoH), from the IDCRP Acute Respiratory Infection Repository Protocol were utilized

Statistical Considerations

- Descriptive statistics are presented. Continuous variables are presented as medians/interquartile ranges and categorical variables as proportions
- Kruskal-Wallis test and Chi-square/Fisher exact test were used to calculate two-sided *p* values for continuous and categorical variables respectively
- Geometric Mean Fold Rise were defined as changes from baseline to first time point post–dose 2
- Geometric Mean Fold Decrease were defined as changes from first time point post dose 2 to the second time point post dose 2

Results

Table 1. Comparison of Characteristics of Responders and Non-Responders

	Overall (n=63)	Non Responders (n=8)	Responders (n=55)
Age	60 (54-67)	58 (51-66)	60 (55-67)
Male sex	52 (83)	7 (88)	45 (82)
Race White Black	 30 (48) 27 (43)	 2 (25) 5 (63)	 28 (51) 22 (40)
CD4 count (cells/uL)	645 (483-859)	525 (105-640)	687 (487-873)
Nadir CD4 count (cells/uL) [1]	180 (91-291)	81 (24-152)	213 (100-304)
Viral load (copies/mL) [1]	20 (20-20)	25 (20-146416)	20 (20-20)
ART use [1]	60 (95)	6 (75)	54 (98)
Zostavax use [2]	30 (47.6)	1(12.5)	29(52.7)
Anti gE IGG [1]	8906 (6294-12601)	29568 (10427-83848)	7479 [5283-10589]
BMI Overweight Obese	 25 (39.7) 14 (22.2)	 2 (25) 4 (50)	 23 (42) 10 (18.2)

1- p<0.05; 2- p=0.05 to 0.10

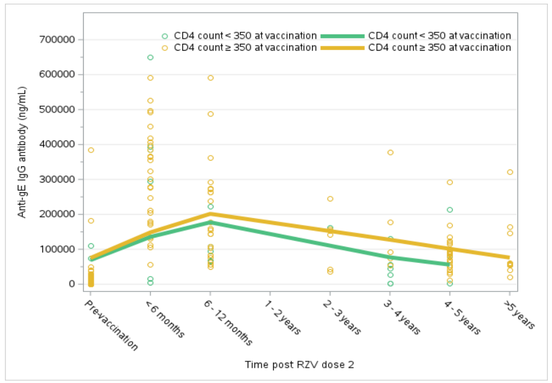


Figure 1. Anti-gE IgG Ab Over Time Stratified by CD4 count < 350 and ≥ 350 cells/µL Prior to Receipt of Dose 1

Results (cont.)

Table 2. Characteristics of Vaccine Responders, Stratified by Whether Responses were Sustained at the Second post-2nd RZV Measurement

	Overall (n=45)	Increase not sustained (n=12)	Sustained increase (n=33)
Age [2]	59 (55-65)	64 (58-72)	57 (54-62)
Male sex	36 (80)	11 (92)	25 (76)
Race White Black	 23 (51) 17 (38)	 7 (58) 4 (33)	 25 (76) 8 (24)
CD4 count (cells/uL)	697 (569-873)	630 (396 -713]	716 (569-894)
Nadir CD4 count (cells/uL)	180 (99 -304)	177 (82-278)	180 (102-309)
Viral load (copies/mL)	20 (20-20)	20.0 (20-20)	20 (20-20)
ART use	44 (98)	0	1 (3)
Live zoster vaccine	27 (60)	8 (67)	19 (58)
Anti gE IGG [1]	6826 (4511-10330)	26933 (17675-41041)	4144 (2688-6389)
BMI Overweight Obese	 19 (42) 7 (16)	 5 (42) 4 (33)	 14 (42) 3 (9)

1- p<0.05; 2- p=0.05 to 0.10

Table 3. Geometric Mean Fold Rise (GMFR) and Geometric Mean Fold Decrease (GMFD) in Anti-gE IgG Following RZV Vaccination

CD4 count	N	GMFR [95% CI]	N	GMFD [95% CI]
Current CD4 <T1 (<486 c/uL) T1 to T3 (486 -858 c/uL) >T3 (>858 c/uL)	 16 31 16	 7.7 (6.9 to 8.6) [1] 30.9 (28.0 to 34.1) [1] 31.8 (26.7 to 38.0) [1]	 12 26 14	 2.3 (2.1 to 2.4) 3.2 (3.1 to 3.3) 3.2 (3.2 to 3.3)
Nadir CD4 <T1 (<91 c/uL) T1 to T3 (91-290 c/uL) >T3 (>290 c/uL	 15 31 17	 9.9 (8.2 to 12.0) 24.2 (22.2 to 26.4) 36.7 (30.9 to 43.6)	 13 25 14	 2.6 (2.5 to 2.8) 2.9 (2.8 to 3.0) 3.5 (3.3 to 3.7
Nadir <200 and Current<350	8	5.5 (4.3 to 7.0) [1]	8	2.7 (2.4 to 3.1)
Nadir <200 but Current ≥350	26	26.6 (23.6 to 30.0) [1]	22	2.8 (2.7 to 2.9)

GMFR: geometric mean fold rise in Anti gE IgG comparing pre dose 1 and post dose 2, GMFD: geometric fold decline in Anti gE IgG comparing post dose 2 (time points 1 and 2).
1- p<0.05

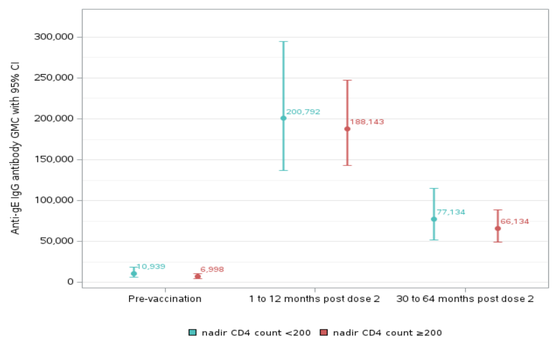


Figure 2- Anti-gE IgG Ab GMC before RZV vaccination, at the 1st and 2nd post-2nd RZV measurements, stratified by nadir CD4 count Prior to Receipt of Dose 1

Discussion

- About **one in seven PWH** failed to achieve a four-fold increase in anti-gE antibodies (in comparison ~5% failed to demonstrate a humoral response in ZOE 50/70)
- Non-responders
  - Had lower nadir CD4 count
  - Were not receiving antiretroviral therapy
  - Had higher HIV viral load
  - Had higher baseline anti-gE antibody levels prior to vaccination
- Responders had more often received the live zoster vaccine and had high pre-vaccination CD4 counts
- The association with prior live vaccine receipt may be confounded by cd4 counts and needs further study
- Ab levels dropped off and at 5 years, **in 25% the response was transient**
- Predictors of waning immunity include older age at vaccination and elevated baseline antibody titers
- CD4 counts ≥350 cells/µL at RZV receipt was associated with improved response
- Failure to reconstitute immunologically (i.e. nadir CD4 <200 and current CD4<350 cells) led to an attenuated response

Conclusions

Optimal Timing of RZV in PWH Needs Study
RZV response maybe optimized if administered after ART initiation, viral suppression, and CD4 reconstitution

Durability Concerns
Humoral responses declined between 3-5 years post-RZV in PWH, raising concerns about durability and need for boosters

Future Research Priorities
Studies examining vaccine effectiveness in PWH are needed especially in those with low CD4 counts (<350 cells/uL) at RZV administration

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