IgG2 antibody response to a prime-boost vaccine strategy combining PCV13 followed by PPV23 versus PPV23 alone in HIV-infected adults

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Background

- *Strep. pneumoniae* remains one of the most significant causes of morbidity and mortality worldwide
- HIV infected adults are disproportionately affected[1,2]
- IPD - associated mortality of 10-50%[3,4]

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2.Jordano Q. Clin Infect Dis 2004; 38:1623
3.Grau I. Arch Intern Med 2005; 165:1533
4.Scarborough M. N Engl J Med 2007; 357:2441

Aim

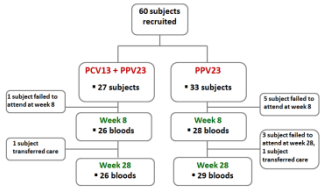
- In this single centre randomised controlled trial, we compared IgG2 subclass response to a prime boost vaccine strategy combining the 13-valent conjugate pneumococcal vaccine (PCV13) followed by the 23-valent polysaccharide pneumococcal vaccine (PPV23) versus PPV 23 alone in HIV-infected adults.

Study Plan

- HIV-infected adults ≥18 years, pneumococcal vaccine naïve wit CD4 count > 200 cells/mm³ were recruited
- Randomised to receive PCV13 + PPV23 at week 4 or PPV23

Week 0	Week 4	Week 8	Week 28
PCV13 + PPV23 group: Pre-dose blood draw + PCV 13 vaccine	**PPV23 group:** Pre-dose blood draw **Both groups:** PPV23 vaccine	**Both Groups:** 4 week post vaccine blood draw	**Both Groups:** 24 weeks post vaccine blood dr

Disposition of subjects



Patient Characteristics

	TOTAL COHORT	PPV 23	PCV13+PPV23	P-value
N	60	33	27	
Male n, (%)	55 (92)	29 (88)	26 (96)	0.37
Age (mean)[SD]	37 [10]	37 [10]	36 [10]	0.70
Race n, (%)				
Caucasian	48 (80)	25 (76)	23 (85)	0.52
Hispanic	7 (12)	4 (12)	3 (11)	1.0
Black	5 (8)	4 (12)	1 (4)	0.37
Risk of Acquisitions n, (%)				
MSM	49 (82)	25 (76)	24 (89)	0.32
Hetero	8 (13)	6 (18)	2 (8)	0.28
IDU	3 (5)	2 (6)	0	0.49
CD4 + count (mean)[SD]	503 [219]	447 [181]	572 [243]	
On HAART n, (%)	28 (47)	17 (52)	11 (40)	0.45
HIV $\log_{10}$ (mean) [SD]	2.37 [2.1]	2.16 [2]	3 [2]	1.1
Smoker n, (%)	20 (33)	11 (33)	9 (27)	1.0

Results

Overall IgG2 GMT [CI] increased significantly post-vaccination;

- IgG 2 GMT week 0 = 12.08[9.82-14.86]ug/ml
- IgG 2 GMT week 8 = 63.60[51.84-77.52]ug/ml, (p<0.001)
- IgG2 GMT week 28 = 33.08 [26.22-41.73]ug/ml, (p<0.001)

Results

- **At week 8,** 93% of the un-primed and92% of the prime-boost group had a >2 fold increase in IgG2. Fold increase inIgG2 GMT in the un-primed versus prime-boost group was (mean [SD]; 6.35 [3.88] versus 7.04[6.77],p=0.64).
- **At week 28,** 76% of the un-primed group and 68% of the prime-boost group had >2 fold increase in IgG2 (p=0.56). Fold increase in IgG2 GMT in the un-primed versus the prime-boost group was (mean [SD]; 3.55 [2.87] versus 3.56 [2.84], p=0.99).

Conclusions:

- 93% of study participants had a significant IgG2 response at week 8 however by week 28 the proportion of IgG2 responders (72%) along with IgG2 GMT(33.08ug/ml) decrease significantly (p=0.01 and <0.001 respectively).
- This indicates a poor durability of IgG2 antibody protection in this patient cohort.
- There was no detectable difference in magnitude or durability of IgG2 response in the prime-boost versus the un-primed vaccine groups.
- Clinical end-point trials are needed to clarify the optimal pneumococcal vaccine strategy and schedule in HIV-infected adults