

## **Immunogenicity and Safety of the 13-Valent Pneumococcal Conjugate Vaccine versus the 23-Valent Polysaccharide Vaccine in Unvaccinated HIV-Infected Adults: A Pilot, Prospective Controlled Study**

**Objectives:** Definition of the optimal pneumococcal vaccine strategy in HIV-infected adults is still under evaluation. We aimed to compare immunogenicity and safety of the 13-valent pneumococcal conjugate vaccine (PCV13) versus the 23-valent polysaccharide vaccine (PPSV23) in HIV-infected adults.

**Methods:** We performed a pilot, prospective controlled study enrolling HIV-infected pneumococcal vaccine-naïve outpatients, aged 18-65 years with CD4 counts  $\geq 200$  cells/ $\mu$ L. Eligible subjects were recruited into two parallel groups: group 1 (n = 50) received two doses of PCV13 eight weeks apart, and group 2 (n = 50) received one dose of PPSV23, as part of their standard of care. Anti-pneumococcal capsular polysaccharide immunoglobulin G concentrations were quantified by ELISA at baseline, 8, 24 and 48 weeks. Clinical and viro-immunological follow-up was performed at the same time points. Unvaccinated, age-matched HIV-negative adults (n = 100) were also enrolled as baseline controls.

**Results:** Pre-vaccination specific IgG titers for each pneumococcal antigen did not differ between study groups but they were constantly lower than those from the HIV-negative controls. After immunization, significant increases in IgG titers were observed in both study groups at each time point compared to baseline, but response to serotype 3 was blunted in group 1. Antibody titers for each antigen did not differ between study groups at week 48. Overall, the proportion of subjects achieving seroprotection and seroconversion to all serotypes was comparable between groups. A marked decrease in IgG levels over time was observed with both vaccines. No relevant adverse reactions were reported in either group.

**Conclusions:** In this population with favorable immune profile, no relevant differences were observed in immunogenicity between PCV13 and PPSV23. Both vaccines were safe and well tolerated.

## **Long-Term Serological Response to 13-Valent Pneumococcal Conjugate Vaccine Versus 23-Valent Polysaccharide Vaccine in HIV-Infected Adults**

**Introduction:** Long-term comparative immunologic response to 13-valent pneumococcal conjugate vaccine (PCV13) versus 23-valent polysaccharide vaccine (PPV23) among HIV-infected adults has not yet been investigated.

**Methods:** In this prospective pilot study, we quantified in HIV-positive adults serotype-specific IgG concentrations of the 12 pneumococcal serotypes shared by both vaccines 5 years after vaccination with two doses of PCV13 8 weeks apart (group 1) or one dose of PPV23 (group 2) and compared them with those assessed prior to vaccination (BL) and after 1 year (T1). Comparison of immunogenicity was based on geometric mean concentration (GMC), proportion of individuals with  $\geq$  twofold increase from BL in specific antibody concentration against  $\geq 2$  serotypes and percentage of individuals with serotype-specific IgG  $\geq 0.35 \mu\text{g/ml}$ ,  $\geq 1 \mu\text{g/ml}$  and  $\geq$  individual serotype-specific correlates of protection.

**Results:** We included 91 subjects (median CD4+ 650 cells/ $\mu\text{l}$ ,  $> 90\%$  with HIV-RNA  $< 50$  copies/ml); patients in groups 1 (n = 42) and 2 (n = 49) were homogeneous for the main characteristics. GMCs were significantly higher in the PCV13 group than in the PPV23 group for serotype 19F (p = 0.003). Both vaccines revealed higher significant GMCs to most serotypes compared with BL, i.e., eight in group 1 vs. seven in group 2. With respect to T1, GMCs decreased significantly in the PCV13 group for eight vs. ten serotypes in the PPV23 group. More participants in the PCV13 group had  $\geq 2$  increase from BL in antibody levels to  $\geq 2$  serotypes compared with the PPV23 group (78.6% vs. 59.2%, p = 0.042). Overall, the percentage of subjects with serotype-specific IgG  $\geq 0.35 \mu\text{g/ml}$ ,  $\geq 1 \mu\text{g/ml}$  and  $\geq$  individual serotype-specific correlates of protection was similar between groups.

**Conclusion:** In this study with HIV-positive adults with a favorable viro-immunologic profile, both vaccines were shown to achieve a long-term durable serologic response. We found minor differences in immunogenicity between the two vaccines, which favored PCV13 over PPV23 5 years after immunization.

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### **Nasopharyngeal bacterial and fungal colonization in HIV-positive versus HIV-negative adults**

**Objectives:** To compare mucosal flora in HIV-positive and HIV-negative subjects, to assess chemosusceptibility patterns of carriage isolates and to evaluate possible predisposing factors within the two groups.

**Methods:** We analyzed microbes isolated from nasopharyngeal swabs in virologically suppressed and immunologically stable HIV-positive adult outpatients (n=105) at baseline and after 12 months and in an age-matched cohort of HIV-negative outpatients (n=100) at baseline. Bacteria and Candida spp strains were isolated and identified through standard biochemical assays and chemosusceptibility tests were performed. Multi Locus Sequence Typing was also determined to characterize Staphylococcus aureus isolates from HIV-infected persistent carriers.

**Results:** In HIV-positive patients a significantly higher rate of colonization by *S. aureus* as compared to HIV-negative controls was observed (19% vs 8%,  $p=0.02$ ), with a relevant percentage of penicillin resistant strains (15% vs 0,  $p=0.24$ ). Methicillin resistant strains were recovered only from HIV-positive subjects. Overall HIV-positive status was the only predictor of *S. aureus* colonization (OR 2.77, 95% CI 1.03;7.41,  $p=0.04$ ).

**Conclusions:** The nasopharyngeal bacterial flora differs between HIV-positive and HIV-negative subjects and appears relevant for possible development of staphylococcal infections in HIV-positive patients.