

# Role of Pneumococcal Vaccine in HIV Infected Population

Ram Gopalakrishnan<sup>1</sup>

Severe and recurrent pneumococcal disease is more common with HIV infection.<sup>1-3</sup> Adults infected with human immunodeficiency virus (HIV) are at high risk for *Streptococcus pneumoniae* infections as a result of humoral immune dysfunction. The reported incidence rates of invasive pneumococcal disease in HIV-infected adults range from 197 to 5700 per 100,000 person-years, which are 6- to 324-fold higher than rates for uninfected adults.<sup>1</sup> Given the increased risk for pneumococcal disease, vaccination with the pneumococcal conjugate vaccines reduce vaccine-type invasive pneumococcal disease and radiographically-confirmed pneumonia in children with HIV.<sup>4</sup> In addition, the 7-valent pneumococcal conjugate vaccine was effective against vaccine-type invasive pneumococcal disease in a randomized controlled trial of HIV-infected adults with a recent history of pneumococcal disease.<sup>5</sup>

## Immunogenicity and safety data of PCV13 in HIV infected adults

The 13-valent pneumococcal conjugate vaccine has been added to existing recommendations for pneumococcal vaccination of immunocompromised populations.<sup>6-9</sup>

In an open label study,<sup>10</sup> 329 HIV infected adults previously vaccinated with PPSV23 were assessed for safety and immune response to 3 doses of PCV13. It appeared that PCV13 was safe and immunogenic in HIV infected adults with CD4 counts  $\geq$  200 cells/mm<sup>3</sup>.

## Efficacy of PCV7 And PPV23 in IPD and all-cause pneumonia

Two studies conducted by the

same investigator examined the efficacy of PPSV23 and PCV7, each versus placebo, in preventing IPD and pneumonia in patients with HIV.<sup>5,11</sup> The first large, randomized, placebo-controlled trial was conducted to study the efficacy of PPV23 in young Ugandan (Africa) adults with HIV infection.<sup>11</sup> A total of 1,392 HIV-infected adults were randomized to receive PPV23 or placebo. Vaccine-type IPD and all-cause pneumonia were greater in the vaccine group than the placebo group during the first 6 months of follow-up and were not statistically different from the control group after the prescribed 2.5 years of follow-up (VT-IPD relative risk of 1.48, 95% CI: 0.65-3.32; all-cause pneumonia relative risk of 2.02, 95% CI: 1.19-3.45). The authors concluded that PPV23 is ineffective in HIV-1-infected Ugandan adults and probably has little, or no, public health value elsewhere in sub-Saharan Africa. After 10 years, a second randomized, placebo-controlled trial compared PCV7 to placebo at a single hospital in Malawi.<sup>5</sup> All study participants had recovered from a documented case of IPD in the past, were 15 years of age or older, and had to have been willing to undergo an HIV test. Enrolled subjects received two doses of PCV7 or placebo 4 weeks apart and were followed every 3 months. The unadjusted vaccine efficacy in prevention of additional episodes of vaccine serotype and 6A serotype associated IPD was 74% (95% CI: 30, 90) in participants with a positive HIV test (Hazard

Ratio [HR]: 0.26, 95% CI: 0.1, 0.7) and 73% (95% CI: 23, 89) in all enrolled participants (including those without HIV infection). In a subgroup of 220 patients who were severely immunocompromised (CD4+cell count < 200 cells/mm<sup>3</sup> at baseline), the vaccine efficacy was 86% (95% CI 41-97). The unadjusted vaccine efficacy for first all-cause pneumonia, the secondary endpoint, was 25% (95% CI: -19%, 53%). Although this result did not achieve statistical significance, it reveals a promising trend for reduction of CAP in an immunocompromised population. The authors concluded that PCV7 protected HIV-infected adults from recurrent pneumococcal infection caused by vaccine serotypes or serotype 6A.

## References

1. Bliss SJ, O'Brien KL, Janoff EN, et al. The evidence for using conjugate vaccines to protect HIV-infected children against pneumococcal disease. *Lancet Infect Dis* 2008;8:67-80
2. Wolter N, Cohen C, Tempia S, et al. HIV and influenza virus infections are associated with increased blood pneumococcal load: a prospective, hospital-based observational study in South Africa, 2009-2011. *J Infect Dis* 2014;209:56-65.
3. McEllistrem MC, Mendelsohn AB, Pass MA, et al. Recurrent invasive pneumococcal disease in individuals with human immunodeficiency virus infection. *J Infect Dis* 2002;185:1364-8.
4. Klugman KP, Madhi SA, Huebner RE, et al. A trial of a 9-valent pneumococcal conjugate vaccine in children with and those without HIV infection. *N Engl J Med* 2003;349:1341-8.
5. French N, Gordon SB, Mwalukomo T, et al. A trial of a 7-valent pneumococcal conjugate

<sup>1</sup>Senior Consultant, Institute of Infectious Diseases, Apollo Hospitals, Chennai; Adjunct Professor, Tamil Nadu Dr. MGR Medical University; Adjunct Associate Professor, Apollo Hospitals Educational and Research Foundation.

vaccine in HIV-infected adults. *N Engl J Med* 2010;362:812-22.

6. CDC. Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morbidity and mortality weekly report* 2012;61:816-9.
7. ATAGI. 4.13.7 Pneumococcal Disease: Recommendations. The Australian Immunization Handbook 10th Edition 2013. 10th ed: Australian Government Department of Health and Ageing, 2013.
8. Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host. *Clin Infect Dis* 2014;58:309-18.
9. Tomczyk S, Bennett NM, Stoecker C, Gierke R, Moore MR, Whitney CG, et al. Use of PCV-13 and PPSV-23 vaccine among adults aged 65 and older: recommendations of the ACIP Morbidity and Mortality Weekly Report. 2014;63;822-825
10. Glesby MJ, Brinson CC, Greenberg RN, Lalezari JP, Scott DA, Thoma BS et al. Immunogenicity and safety of 13-valent pneumococcal conjugate vaccine in HIV+ Adults with prior 23-valent pneumococcal polysaccharide vaccination. Presented at the 20th Conference on retroviruses and opportunistic infections (CROI); Atlanta, GA, USA; March 3-6, 2013
11. French N, Nakiyingi J, Carpenter LM, et al. 23-valent pneumococcal polysaccharide vaccine in HIV-1-infected Ugandan adults: double-blind, randomised and placebo controlled trial. *Lancet* 2000;355:2106-11.