



## Commentary

# Pneumococcal vaccination in persons living with HIV: Pneumococcal conjugate, polysaccharide or both?

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Persons living with HIV (PLWH) have a persistent immune-deficient state, created by depletion of CD4 cells, even in those who are on combination Anti-retroviral therapy. This predisposes them to a host of opportunistic infections, of which *Streptococcus pneumoniae* is an important pathogen. Invasive Pneumococcal Disease (IPD) and pneumococcal pneumonia continue to pose a challenge with high recurrence rates [1], significant public health impact, morbidity and high mortality rate of up to 25% in them [2]. The introduction of pneumococcal vaccines (Pneumococcal Conjugate vaccine: PCV 13 and Pneumococcal poly-saccharide vaccine: PPSV23) has significantly helped in reducing the morbidity, but this group still remains at 30 times higher risk of IPD as compared to the healthy adults. The level of immunosuppression (CD4 count <200 cells/ $\mu$ L) and high levels of HIV RNA have been strongly associated with the risk of IPD [3].

The immune response induced by PPSV23 is a T-cell independent humoral response, while PCV13 induces a T-cell-dependent response producing pneumococcal serotype (PS)-specific antibodies and memory B cells (MBCs) which provide long-lasting protection [4]. Sequential vaccination with PCV 13 followed by PPSV 23 provides a prime boost effect on inducing and maintaining protective immunity [5]. These vaccines are less immunogenic in PLWH as compared to healthy adults due to a mitigated immune response. The combination of PPSV23 and PCV 13 has been shown to be more immunogenic, than either of the vaccines alone, and is recommended internationally for prevention of IPD in PLWH [6].

However, despite such international guidelines, the uptake and receptivity towards pneumococcal vaccines is far from satisfactory in this group [7]. Moreover, the dearth of clinical efficacy trials, as these require a mammoth sample size, regular and frequent follow ups over a prolonged time period, complex study designs and logistics/feasibility issues, make immunogenicity studies the only viable surrogate marker to assess the efficacy and utility of these vaccines. The clinical trials evaluating the efficacy of pneumococcal vaccine in

patients with HIV have been majorly carried out in the global south, while the global north has largely contributed observational studies.

In EClinicalMedicine, the systematic review and meta-analysis by Abraham Goorhuis et al. [8] looks into the available literature on immunogenicity of pneumococcal vaccination in PLWH, after combination ART became available in 2000 [9]. It is interesting that out of 1597 study unique studies only 19 could be included for the final meta-analysis. Despite significant heterogeneity in the findings in these studies, these authors found that the overall pooled seroconversion rates (SCR), (defined as a response to > 50% of serotypes, 1–3 months after vaccination with PCV, PPSV23 or their combination, in adult PLWH) were 42%, 44% and 57% for PLWH who received PPSV, PCV20 or a combination of PCV/PPSV, respectively. The authors conclude that the literature is deplete of good quality studies. In this meta-analysis the authors found only 2 randomized controlled trials (RCTs) and 5 cohort studies to be of good quality from a total of 39 eligible studies included for analysis. The assessment parameters used and the serotypes studied are only a handful and variable in different studies. There is paucity of data on serotype specific response studies, especially for PPSV. The overall SCR for PPSV 23 (8.3–93%), PCV (22–86%) and for PCV/PPSV23 combination (51–100%) were lower than those seen in HIV negative adults (86–100%) reflecting better immunogenicity in HIV negative population. The overall SCR is to the tune of 57% which is similar to those reported in other immunodeficient states (59%) [10]. This the PLWH were more likely to achieve good SCR when immunized with PCV/PPSV23 combination than either of the vaccine administered alone.

The authors found from the analysis that serotype 14 was more immunogenic than serotype 6B. Better immunogenic responses were observed in individuals with higher CD4 counts at vaccination and suppressed viral loads. Only three studies looked into long term (> 5 years) immunogenicity of the individual vaccines without encouraging results.

Concerted efforts need to be directed towards targeted research in establishment of a uniform definition of seroconversion and correlates of protection. Studies evaluating long term immunogenicity,

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planned with scientific rigour are the need of the hour. Improved diagnostic assays and advancements in the field of vaccine development might be a harbinger of change in the lives of PLWH. With higher valent pneumococcal vaccines on the anvil (e.g. PCV20), providing coverage against extended number of serotypes, the vaccination recommendations in this group of people will need to be reconsidered and optimized.

#### Declaration of Competing Interest

The authors have nothing to disclose.

#### References

- [1] Grau I, Ardanuy C, Linares J, Podzamczar D, Schulze MH, Pallares R. Trends in mortality and antibiotic resistance among HIV-infected patients with invasive pneumococcal disease. *HIV Med* 2009;10:488–95.
- [2] van Aalst M, Lotsch F, Spijker R, et al. Incidence of invasive pneumococcal disease in immunocompromised patients: a systematic review and meta-analysis. *Travel Med Infect Dis* 2018;24:89–100.
- [3] French N, Gordon SB, Mwalukomo T, et al. A trial of 7-valent pneumococcal conjugate vaccine in HIV-infected adults. *N Engl J Med* 2010;362:812.
- [4] Clutterbuck EA, Lazarus R, Yu LM, et al. Pneumococcal conjugate and plain polysaccharide vaccines have divergent effects on antigen-specific B cells. *J Infect Dis* 2012;205:1408–16.
- [5] Farmaki PF, Chini MC, Mangafas NM, et al. Immunogenicity and immunological memory 15 induced by the 13-valent pneumococcal conjugate followed by the 23-valent polysaccharide 16 vaccine in HIV-infected adults. *J Infect Dis* 2018;218(1):26–34.
- [6] Lopez A, Mariette X, Bachelez H, et al. Vaccination recommendations for the adult 20 immunosuppressed patient: a systematic review and comprehensive field synopsis. *J Autoimmun* 2017;80:10–27.
- [7] Valour F, Cotte L, Voirin N, et al. Vaccination coverage against hepatitis A and B viruses, 26 *Streptococcus pneumoniae*, seasonal flu, and A(H1N1)2009 pandemic influenza in HIV-infected 27 patients. *Vaccine* 2014;32(35):4558–64.
- [8] Garcia Garrido HM, Schnyder JL, Tanck MWT, et al. Immunogenicity of pneumococcal vaccination in HIV infected individuals: 1 a systematic review and meta-analysis. *Eclin Med* 2020. doi: 10.1016/j.eclinm.2020.100576.
- [9] van Aalst M, Langedijk AC, Spijker R, de Bree CJ, Grobusch MP, Goorhuis A. The effect of 17 immunosuppressive agents on immunogenicity of pneumococcal vaccination: a systematic review and 18 meta-analysis. *Vaccine* 2018;36(39):5832–45.
- [10] Carpenter CC, Cooper DA, Fischl MA, et al. Antiretroviral therapy in adults: updated 16 recommendations of the International AIDS Society–USA Panel. *JAMA* 2000;283(3):381–90.