**Safety and Immunogenicity of V114, a 15-Valent Pneumococcal Conjugate Vaccine (PCV), in Adults Infected With Human Immunodeficiency Virus (HIV): A Phase 3 Trial**

**Introduction**
- Individuals infected with human immunodeficiency virus (HIV) are at an increased risk of pneumococcal disease (PD) compared with uninfected individuals.
- In many countries, vaccination against PD is recommended for adults infected with HIV, irrespective of an individual’s CD4+ T-cell count.
- Sequential vaccination with 15-valent pneumococcal conjugate vaccine (PCV15) followed by the 23-valent pneumococcal polysaccharide vaccine (PPSV23) may be indicated, and is at least of equal or better vaccine efficacy compared with PPSV23 alone.
- Despite the success of PCVs in reducing PD caused by Streptococcus pneumoniae serotypes covered by currently available pneumococcal vaccines, the prevalence of PD caused by serotypes not covered by these vaccines remains a concern.
- V114, a 15-valent pneumococcal conjugate vaccine containing 15 serotypes not covered by PCV13 (1, 3, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F), was developed to provide broader serotype coverage.
- This phase 3 trial evaluated the immunogenicity and safety of V114 followed by PPSV23 8 weeks later in adults infected with HIV.

**Methods**
- **Study Design**
  - Phase 3, multicentre, randomised, double-blind, active comparator-controlled study.
  - All randomised participants (N=302) received either V114 or PCV13, and 298 participants received both vaccines.
  - Safety profile following PCV13 administration.
  - Immunogenicity:
    - Serotype-specific geometric mean fold-rises from baseline, proportions of participants with titre 
      serotypes unique to V114.
    - Solicited systemic AEs (Day 1 to Day 14 post-PPSV23).

**Study Objectives**
- **Primary Objectives**
  - Safety profile following V114/PCV13 administration:
    - Solicited injection site adverse events (AEs) (Day 1 to Day 5).
  - Solicited systemic AEs (Day 1 to Day 14).

**Safety profile following PPSV23 administration:
- Solicited injection site AEs (Day 1 to Day 5 post-PPSV23).
- Solicited systemic AEs (Day 1 to Day 14 post-PPSV23).
- Vaccine-related serious adverse events (SAEs) (Day 1 to Week 6).
- **Immunogenicity:**
  - Serotype-specific geometric mean fold-rises from baseline.
  - Proportion of participants showing seroconversion.
  - Proportion of participants showing seroconversion for serotypes unique to V114.

**Results**
- **Participant Disposition**
  - All randomised participants (N=302) received either V114 or PCV13, and 298 participants (99.3%) received both vaccines (Table 1).
  - The number of study discontinuations and the reasons for study discontinuations were generally comparable across vaccine groups.
- **Participant Demographics and Baseline Characteristics**
  - Demographic and baseline characteristics were generally comparable for participants across vaccination groups (Table 2).
  - Most participants were male and aged between 18 and 49 years.

**Table 1. Participant Disposition Across Intervention Groups**

<table>
<thead>
<tr>
<th>V114/PCV13</th>
<th>Vaccine-Received (V114)</th>
<th>Vaccine-Received (PCV13)</th>
<th>Total Discontinued</th>
<th>Total Discontinued %</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>150</td>
<td>300</td>
<td>1</td>
<td>0.33%</td>
</tr>
</tbody>
</table>

**Table 2. Participant Demographics and Baseline Characteristics**

<table>
<thead>
<tr>
<th>Age (years), n (%)</th>
<th>HIV viral load results, n (%)</th>
<th>CD8+ T-cell count, n (%)</th>
<th>Race, n (%)</th>
<th>Ethnicity, n (%)</th>
<th>Race, n (%)</th>
<th>Ethnicity, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-49, n=298</td>
<td>≥200 to &lt;500 cells/µL</td>
<td>&lt;500 cells/µL</td>
<td>Male, n=190</td>
<td>Single, n=152</td>
<td>Male, n=190</td>
<td>Single, n=152</td>
</tr>
</tbody>
</table>

**Conclusions**
- In pneumococcal vaccine-naive adults infected with HIV:
  - Vaccine was well-tolerated.
  - V114 induces immune responses to all 15 pneumococcal serotypes, as assessed by OPA GMTs and IgG4 titres.
  - There is a trend toward higher serotype-specific OPA GMTs and IgG4 titres at 12 weeks post-vaccination with V114 in participants with CD4+ T-cell count ≥500 cells/µL, and undetectable viral load versus those with CD4+ T-cell count <500 cells/µL, and detectable viral load.
  - V114 can be followed by PPSV23 in 8 weeks, as the immune response for shared serotypes and accumulated antibodies was well tolerated.

**References**