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Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine compared to a 23-valent pneumococcal polysaccharide vaccine in pneumococcal vaccine-naive adults☆

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ABSTRACT

Background: Streptococcus pneumoniae is a major cause of morbidity and mortality among adults 50 years of age and older in the United States. Pneumococcal conjugate vaccines are efficacious against pneumococcal disease in children and may also offer advantages in adults.
Methods: We performed a randomized, modified double-blind trial that compared a single dose of 13-valent pneumococcal conjugate vaccine (PCV13) with 23-valent pneumococcal polysaccharide vaccine (PPSV23) in 831 pneumococcal vaccine naive adults 60–64 years of age. An additional group of 403 adults 50–59 years of age received open-label PCV13. Anti-pneumococcal opsonophagocytic activity (OPA) titers were measured at baseline, and at 1 month and 1 year after vaccination.
Results: In the randomized trial, the month 1 post-vaccination OPA geometric mean titers in the PCV13 group were statistically significantly higher than in the PPSV23 group for 8 of the 12 serotypes common to both vaccines and for serotype 6A, a serotype unique to PCV13, and were comparable for the other 4 common serotypes. The immune response to PCV13 was generally greater in adults 50–59 years of age compared to adults 60–64 years of age. OPA titers declined from 1 month to 1 year after PCV13 administration but remained higher than pre-vaccination baseline titers.
Conclusions: PCV13 induces a greater functional immune response than PPSV23 for the majority of serotypes covered by PCV13, suggesting that PCV13 could offer immunological advantages over PPSV23 for prevention of vaccine-type pneumococcal infection.

Abbreviations: AE, adverse event; CI, confidence interval; CRM197, cross-reactive material 197; GMR, geometric mean ratio; GMT, geometric mean titer; IPD, invasive pneumococcal disease; LLOQ, lower limit of quantitation; LOD, limit of detection; OPA, opsonophagocytic activity; PCV, pneumococcal polysaccharide conjugate vaccine; PCV7, 7-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; PPSV23, 23-valent polysaccharide vaccine; RCDC, reverse cumulative distribution curve; SAE, serious adverse event.

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1. Introduction

Streptococcus pneumoniae is a major cause of morbidity and mortality among older adults in the United States. Currently in the United States the 23-valent pneumococcal polysaccharide vaccine (PPSV23) is recommended for adults 65 years of age and older, as well as for high-risk younger adults, for prevention of invasive pneumococcal disease (IPD) [1,2]. However, PPSV23 has some limitations. While the vaccine is believed to be moderately effective in prevention of IPD in immunocompetent older adults, effectiveness wanes over time, and a protective effect against non-bacteremic pneumococcal pneumonia has not been consistently demonstrated [3]. In contrast, pneumococcal conjugate vaccines (PCVs) are highly effective against vaccine-type IPD in children and have also been shown to reduce the risk of all-cause pneumonia. In addition, a 7-valent PCV (PCV7) has been shown to be effective against vaccine-type IPD in a randomized controlled trial of HIV-infected adults. These data suggest potential advantages for the use of PCVs compared to PPSV23 in older adults [4–8].

We conducted a randomized trial to compare the immunogenicity, tolerability, and safety of a 13–valent PCV (PCV13) with PPSV23 in pneumococcal vaccine-naive adults 60–64 years of age. In addition, a cohort of subjects 50–59 years of age received a single dose of open-label PCV13 to compare immune responses between the younger and older age groups.

2. Methods

2.1. Study design and populations

This was a randomized, modified double-blind, multicenter phase 3 trial of adults 60–64 years of age conducted in the USA in 25 medical centers. This study was undertaken in accordance with the Declaration of Helsinki and Good Clinical Practice [9,10]. The study population included persons with pre-existing underlying chronic conditions (e.g. cardiovascular, pulmonary, renal, liver diseases including alcoholic liver disease and alcoholism, and diabetes mellitus). Disease had to be stable, defined as not requiring significant change in therapy or hospitalization for worsening disease 12 weeks prior to vaccination. Participants were excluded if they had serious chronic disorders including metastatic malignancy, severe chronic obstructive pulmonary disease requiring supplemental oxygen, end-stage renal disease with or without dialysis, clinically unstable cardiac disease, impaired immune function, or had previously received a PPSV23 dose or any prior PCV.

After obtaining informed consent, eligible subjects were randomized with equal probability to receive PCV13 or PPSV23 at the enrollment visit. In the modified double-blind design, the vaccines were dispensed and administered by unblinded study staff members not involved in subsequent participant assessments. All other study staff members and participants were blinded to the vaccine administered. Participants 50–59 years of age received a single dose

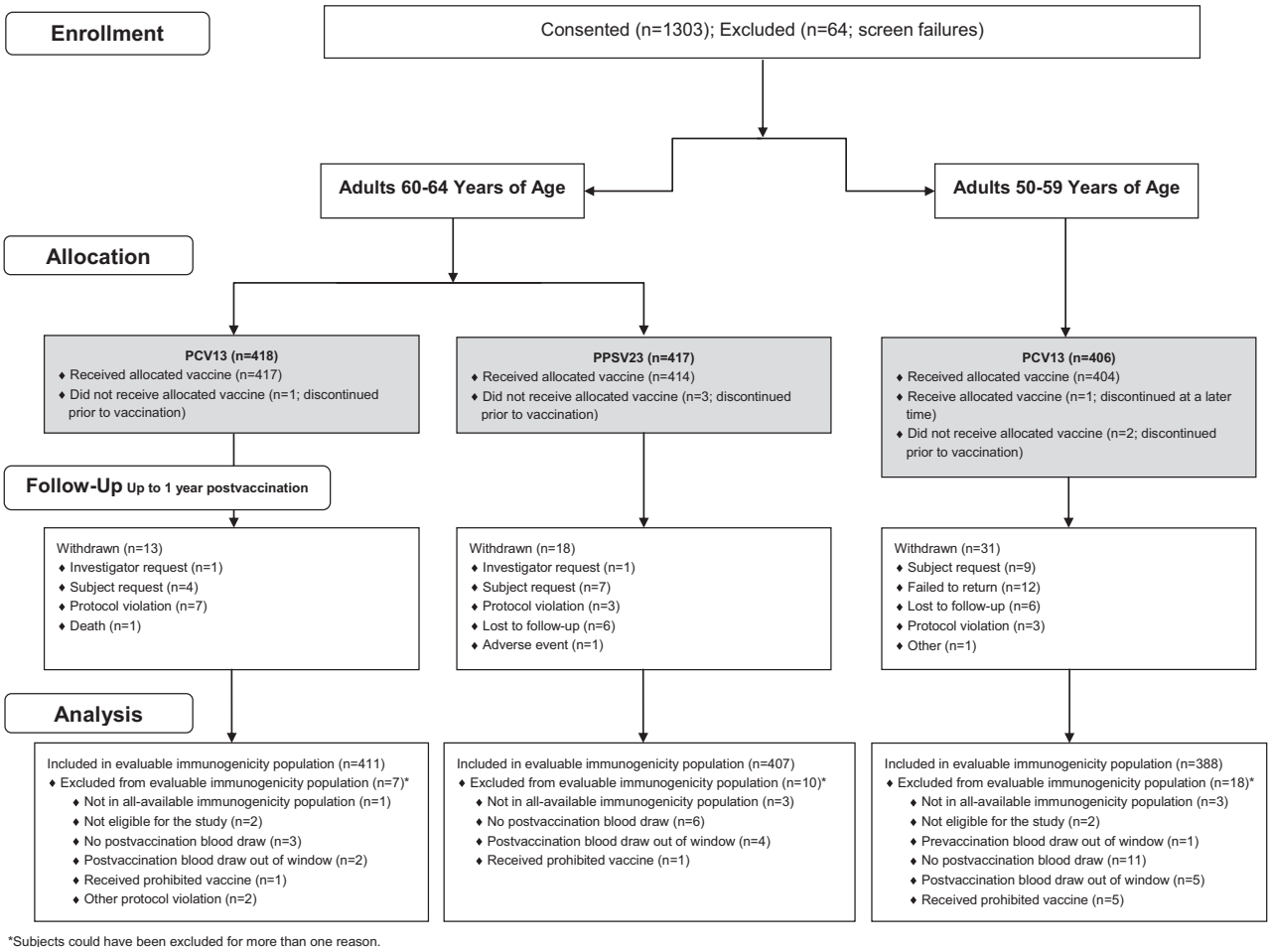

Fig. 1. Study design and disposition of subjects.