A Post-Hoc Analysis Of Immunogenicity Of 13-Valent Pneumococcal Conjugate Vaccine In Subjects With Underlying Medical Conditions in Community Acquired Pneumonia Immunization Trial in Adults (CAPITA)

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Introduction

• Pneumococcal disease is a major global public health problem affecting all age groups. The highest rates of pneumococcal disease occur in young children and in the elderly. Persons older than 50 years of age, particularly those older than 65 years, are at increased risk for developing pneumococcal infection or experiencing severe manifestations.

• The Community Acquired Pneumonia Immunization Trial in Adults (CAPITA), which was randomized, double-blind placebo-controlled, and conducted in persons aged 65 years and older in the Netherlands, demonstrated the efficacy of 13-valent pneumococcal conjugate vaccine (PCV13) against first episodes of vaccine type (VT) pneumonia-causing pneumococcal (PP)-and first episodes of invasive pneumococcal disease. Results of the primary and secondary endpoints as well as safety have been previously reported. Immunogenicity results for a subset of subjects reported during home visits have also been reported. Global vaccine technical committees are now reviewing these efficacy data to define appropriate pneumococcal vaccination strategies for these subjects at risk of pneumococcal pneumonia due to age and/or underlying medical conditions. Therefore, understanding whether immunocompetent adults with underlying medical conditions respond differently to PCV13 when compared with healthy adults aged 65 years and older (the CAPITA study was not stratified in design, nor powered to evaluate immunogenicity or efficacy findings in such subgroups; thus, findings should be viewed as exploratory in nature to be keeping with the description in Koch and Todd).

Objective

• The objective of this analysis was to assess the immune responses of subjects to PCV13 compared with placebo before vaccination and approximately 1, 2, and 24 months after vaccination in subjects with underlying medical conditions or splenectomy.

Study Design

• Approximately 2000 of the 84,496 subjects were recruited at home visits in a single region in the Netherlands, of whom 1688 met criteria and were included in the analysis; 52% were men, 68% were Caucasian, and 62% were aged 65-74 years. Subjects reporting the following medical conditions were included: asthma; diabetes mellitus with and without insulin use; heart disease; liver disease; lung disease; and splenectomy.

• Baseline characteristics and comorbid conditions are shown in Table 1.

Methods

• Immunogenicity Analyses:

• 2011 subjects were enrolled. TD50 subjects entered criteria for the evaluable immunogenicity population [subjects who were eligible, subject who were in the immunogenicity subset, with no major protocol violations, and with at least one valid and determinate result; no major protocol violations].

• OPA titer results for all vaccine serotypes were similar in subjects with underlying medical conditions and the overall immunogenicity subset population, as well as when compared with the individuals reporting no medical conditions.

• Subjects with and without underlying medical conditions and those that reported 2 or more medical conditions revealed in all 12 vaccines at 1 month post vaccination, were comparable across all serotypes for all conditions except splenectomy, in which there was only one subject that reported splenectomy.

• Between 12 and 24 months, OPA titer declined in all PCV13 vaccinated groups and for all serotypes, but remained above baseline. The rate of decline of OPA titers for all serotypes across all underlying medical conditions was similar.

• IgG antibody responses were similar across all evaluated underlying medical conditions and all serotypes across all evaluated time points.

• Although not shown, over the 2-year follow-up period, levels of both functional antibody titers and IgG antibody concentrations remained above baseline and higher than levels observed in placebo recipients.

Results

• OPD GMTs after PCV13 vaccination were similar in subjects with all evaluated underlying medical conditions for all serotypes and all time points when compared with all subjects, and were compared with those subjects who reported no underlying medical conditions or baseline (Figure 1).

• In the placebo group (not shown), baseline levels remained stable over time with and without underlying medical conditions.

• At baseline (prevacuation), and for all vaccine serotypes, OPA titer were similar in those with underlying medical conditions and the overall immunogenicity subset population, as well as when compared with the individuals reporting no medical conditions.

• Subjects with and without underlying medical conditions, and those that reported 2 or more medical conditions revealed in all 12 vaccines at 1 month post vaccination, were comparable across all serotypes for all conditions except splenectomy, in which there was only one subject that reported splenectomy.

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• IgG antibody responses were similar across all evaluated underlying medical conditions and all serotypes across all evaluated time points.

• Although not shown, over the 2-year follow-up period, levels of both functional antibody titers and IgG antibody concentrations remained above baseline and higher than levels observed in placebo recipients.

• These results are consistent with similar analyses in other PCV13 safety and immunogenicity studies.4

• Based upon these data, it could be expected that vaccine efficacy in immunocompetent adults with underlying medical conditions would be comparable to that observed for the overall study population in the CAPITA (Community Acquired Pneumonia Immunization Trial in Adults) study.

Contraints

• Medical history was reported by subjects at baseline, and did not occur for any changes that may have occurred during the 26-week post vaccination follow-up.

• Subjects with immunocompromising conditions were excluded per the study design.

• 70% of the subjects were <75 years old, and therefore in the younger age range of the age spectrum.

• Arguably, both vaccine and placebo titers were not compared, the study was not designed or powered for these sub-populations. In particular, the efficacy of these condition by subset analyses are not reliable due to the study design, as well as the small numbers of subjects with primary endpoints within the evaluable immunogenicity analysis population.

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Limitations

• PCV13 generates titers of functional antibodies in immunocompetent older adults with underlying medical conditions that are comparable to those generated in healthy older adults.

• Functional antibody responses were similar across all evaluated underlying medical conditions and all serotypes across all evaluated time points.

• Although not shown, over the 2-year follow-up period, levels of both functional antibody titers and IgG antibody concentrations remained above baseline and higher than levels observed in placebo recipients.

• These results are consistent with similar analyses in other PCV13 safety and immunogenicity studies.4

• Based upon these data, it could be expected that vaccine efficacy in immunocompetent adults with underlying medical conditions would be comparable to that observed for the overall study population in the CAPITA (Community Acquired Pneumonia Immunization Trial in Adults) study.