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Pneumococcal vaccine update: New ACIP Recommendations

The Food and Drug Administration (FDA) licensed two new vaccines in 2021, the Pneumococcal 20-valent conjugate vaccine (PCV20) and the PCV15. The trade name for the PCV20 is Prevnar 20™ (developed by Pfizer) and the trade name for the PCV15 is Vaxneuvance (developed by Merck).[1] Both vaccines are to be given intramuscularly as a 0.5mL dose and are indicated for the prevention of invasive disease caused by *Streptococcus pneumoniae* in adults 18 years of age and older.[2,3]

Invasive pneumococcal disease (IPD) poses a significant problem to the healthcare system, particularly for the elderly population. Approximately 50% of the pneumococcal disease burden occurs in adults aged 65 years or older, although this age group comprises only 22% of the entire adult population.[4] From 2018 to 2019, the incidence of IPD in adults 65 and older was 24 per 100,000 population. Among the individuals with IPD, 27% of cases were caused by serotypes contained within the PCV13 vaccine. The additional serotypes specific to PCV15, PCV20, and PPSV23 also contributed to a substantial proportion of the IPD, and are listed in **Table 1**.[5] This surveillance data suggests that the PCV15 and PCV20 could provide an benefit to patients with IPD due to the additional coverage of non-PCV13 serotypes.

Table 1. Proportion of Pneumococcal Serotypes Causing Invasive Pneumococcal Disease by Vaccine

	≥65 YEARS	18-64 YEARS
PCV13 SEROTYPES	27%	30%
PCV15-SPECIFIC[A]	15%	13%
PCV20-SPECIFIC[B]	27%	28%
PPSV23-SPECIFIC[C]	35%	43%

[A]Includes serotypes 22F and 33F
[B]Includes serotypes 8, 10A, 11A, 12F, 15B/15C, 22F, and 33F
[C]Includes serotypes 2, 9N, 17F, and 20

New Recommendations

The Advisory Committee on Immunization Practices (ACIP) is a panel that is comprised of medical and public health experts who are responsible for developing recommendations on the appropriate use of vaccines in the general public.[6] They recommend individuals that are 65 years or older with no previous history of pneumococcal conjugate vaccine or an unknown vaccination history should receive a dose of PCV20 or PCV15. If the PCV15 is used, patients should receive a dose of the PPSV23 at least 1 year later. This recommendation also applies to individuals aged 18 to 64 who have underlying medical conditions or other risk factors, listed in **Table 2**. This recommendation was endorsed by the ACIP in October 2021 with a vote of 15 to 0.[7]

Table 2. Underlying medical conditions or other risk factors for individuals 19 to 64

Alcoholism	Nephrotic syndrome
Chronic heart disease	Generalized malignancy
Chronic liver disease	HIV infection
Chronic lung disease	Hodgkin disease
Cigarette smoking	Immunosuppression
Diabetes mellitus	Leukemia
Cochlear implant	Lymphoma
CSF leak	Multiple myeloma
Chronic renal failure	Solid organ transplant
Congenital or acquired asplenia	Congenital or acquired immunodeficiencies
Sickle cell disease or other hemoglobinopathies	

Evidence for New Recommendations

A phase 3 trial demonstrated an effective immune response one month after individuals 50 years of age or older received the PCV15 or the PCV13 vaccine. Immune response was measured by titers of serotype-specific opsonophagocytic activity (OPA) which is a measure of functional antibody response. The PCV15 vaccine met

noninferiority criteria for the 13 shared serotypes and demonstrated superior immunogenicity for serotypes 22F and 33F which are specific to PCV15.[9]

Another phase 3 trial compared the PCV20 to the PCV13 and demonstrated promising results. The primary outcome of this study was to assess immunogenicity and safety across three different manufacturing lots of the PCV20 in order to demonstrate consistency. A key secondary outcome was the comparison of immune responses to the 13 shared serotypes between the PCV20 and PCV13. Across the three lots, the PCV20 met the prespecified equivalence interval for all 20 serotypes, and when compared to the PCV13 serotypes, the PCV20 met noninferiority criteria.[10]

Safety Data

The PCV15 has demonstrated a safety profile that is in similar to the PCV13, and primarily consists of minor side effects. The most common adverse event in the previously mentioned phase 3 trial was injection site pain. Patients in the PCV15 group experienced the injection site pain more often than the PCV13 group, 54% versus 42.3%, respectively. While the difference in injection site pain was statistically significant, the authors note that this is likely not clinically significant due to the majority of events being reported as mild in severity and only lasting 1 to 3 days.[9] The difference in injection site pain is in line with previous studies assessing PCV15 in comparison to PCV13, but the rationale for increased incidence of injection site pain has yet to be elucidated.[11]

The safety and tolerability of the PCV20 was also demonstrated to be similar to the PCV13. In the phase 3 trial comparing the PCV20 to the PCV13, there were no differences in adverse events experienced one month after vaccination in vaccine-naïve adults aged 18 to 49. The most common adverse events were reported to be pain at injection site, muscle pain, and fatigue. The adverse event that occurred most frequently was injection site pain, with 79% of patients receiving the PCV20 and 76% of patients receiving the PCV13 experiencing this local reaction.[10]

Conclusion

The PCV15 and the PCV20 vaccines were shown to confer immune responses similar to the PCV13, while also providing robust immune responses for the additional serotypes. The immune response against additional serotypes has potential to decrease the burden of IPD. In addition to the added immune response, the PCV15 and PCV20 were shown to be safe with the majority of adverse events limited to injection site pain, fatigue, and myalgias. The PCV20 allows individuals to forgo the subsequent PPSV23 and would decrease the number of vaccinations for individuals that are 65 years of age or older, or in patients that are 19 to 64 with underlying medical conditions. Hospitals should assess their ability to acquire the new pneumococcal vaccines and update policies as appropriate. For aid in implementing such plans, please reach out to your DASON liaison, who will be happy to assist.

Table 3. Serotypes in Available Pneumococcal Vaccines

	Serotype																						
Vaccine	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20
PPSV23	x	x	x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PCV20	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				
PCV15	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x									
PCV13	x	x	x	x	x	x	x	x	x	x	x	x	x											

Green shading indicates added serotypes in relation to PCV13

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