Kinetics of Post-Vaccination Seroprotection to *S. Pneumoniae* for the Immune-Compromised and Vaccine-Naïve Populations

J Mond [1], M Scobie[2], C Tolman[1], J Gruenglas[1], J Martinez [2]
[1]ADMA Biologics, Ramsey, NJ; [2]Immune Diagnostics, Asheville, NC

IDWeek2020
Abstract # 911378

INTRODUCTION

- ***S. pneumoniae*** **infection presents a significant challenge, accounting for 20-38% of hospital-acquired pneumonia (HAP), and the leading cause of community-acquired pneumonia despite availability of effective vaccines[1-3]**
- **Incidence is highest in children under 2 years, the immunocompromised, and elderly[4]**
- **CDC has reported the emergence of antibiotic resistance in ~30% of cases, adding to risk of morbidity and mortality[4]**
- **Nearly 40% of those over 65 years of age are unvaccinated and vulnerable to infection on admission[5]**
- **Prophylactic immunotherapy intervention with standard IVIG may not contain sufficient antibody titers to the pathogen[6]**
- **Passive immunity with a hyperimmune IG as an adjunct to vaccines may provide optimal levels of protective titers required to improve outcomes in these populations**

OBJECTIVE

- **To evaluate whether seroprotective response induced with a pneumococcal conjugate vaccine could rapidly yield protective opsonic levels of antibody within anticipated duration of hospitalization**

METHODS

- **Healthy donors (n=30) were immunized with pneumococcal conjugate vaccine**
- **Blood was drawn on days 0, 3, 7, 10, 14, 21, 28; samples were pooled and tested for presence of functional opsonic antibodies recognizing capsular polysaccharides**
- **Titer was determined based on dilution at which 50% kill is observed**
- **Clearance mechanism of *S. pneumoniae* was based on antibody recognition to pneumococcal capsular polysaccharide and opsonic titers used as an in vitro surrogate to evaluate the efficacy of vaccine**

RESULTS

- **There was little to no opsonic activity against most serotypes on day 0, except for low antibody activity with serotypes 1, 3, 4, and 5**
- **Titers increased, with protective levels achieved by day 10 for most serotypes (except 14 and 18C), peaking at day 14 or after across serotypes (Figure 1)**
- **Average titers rose from log2 titer 2 on day 0 to log2 titer 8 on days 21 and 28. Titers against most serotypes reached log2 10 (titer 1024) or higher**

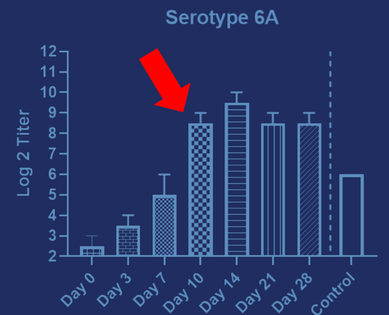

Figure 1. Opsonophagocytic killing (OPK) titers (log2 scale) for serum samples on day 0 (pre), day 3, 7, 10, 14, 21, 28, and control for *S. pneumoniae* serotype 6A.

- **Percent kill curves for drug-resistant serotypes 6A, 14, 19A, and 23A at day 7 are shown (Figure 2)**
- **Antibody response to serotypes 3 and 18C were lowest overall, with day 28 average titers at 7 and 4, respectively. However, antibody titers against most serotypes reached log2 10 (titer 1024) or higher. Prior data indicated that day 7 titers were not sufficiently high enough to be considered protective**

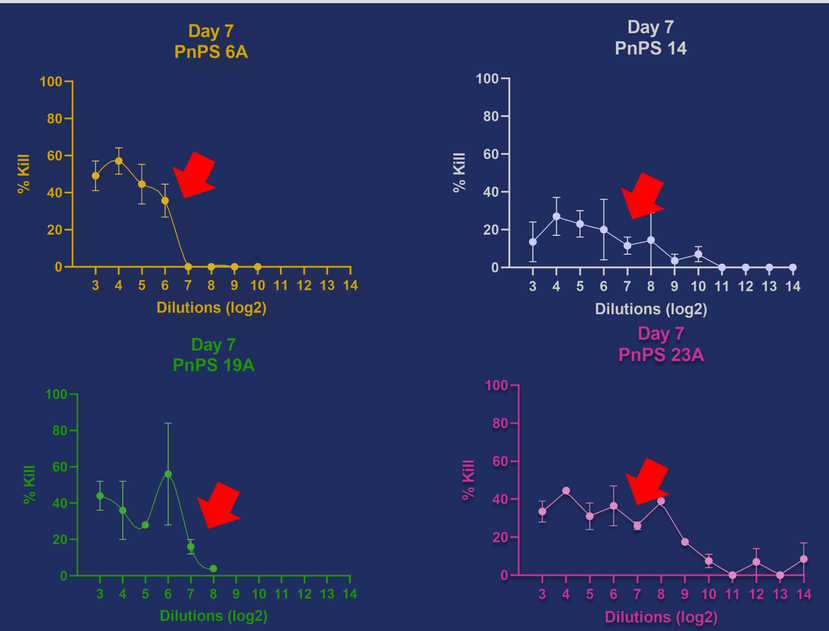

Figure 2. OPK percent kill curves *S. pneumoniae* serotypes 6A (yellow), 14 (blue), 19A (green), and 23A (pink). The x-axis shows sample dilutions started at 1:8 (or 3 on Log2 scale) and serially diluted 1:2 thereafter. The y-axis shows bacterial kill as a percentage of colony forming units (CFUs) from that sample dilutions compared to the CFUs of the complement control.

CONCLUSIONS

- **Patients with no prior history of vaccination (or inability to mount response) with pneumococcal conjugate vaccine or pneumococcal polysaccharide vaccine remain vulnerable to HAP for at least 10 days post admission**
- **Induction of pneumococcal conjugate vaccine demonstrated protective opsonic levels of antibody within anticipated the duration of hospitalization**
- **Prophylactic intervention with a hyperimmune Ig with high opsonic titers to *S. pneumoniae* may offer protection to the patient throughout the hospital stay until vaccine response elicits protective antibodies**

REFERENCES

1. Leone, M. et al. Hospital-acquired pneumonia in ICU. Anaesthesia, critical care & pain medicine 37, 83-98, doi:10.1016/j.accpm.2017.11.006 (2018).
2. Paradisi, F., Corti, G. & Cinelli, R. Streptococcus pneumoniae as an agent of nosocomial infection: treatment in the era of penicillin-resistant strains. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 7 Suppl 4, 34-42 (2001).
3. Mongardon, N. et al. Epidemiology and outcome of severe pneumococcal pneumonia admitted to intensive care unit: a multicenter study. Critical care (London, England) 16, R155, doi:10.1186/cc11471 (2012).
4. Brooks, L. R. K. & Mias, G. I. Streptococcus pneumoniae's Virulence and Host Immunity: Aging, Diagnostics, and Prevention. Front Immunol 9, 1366, doi:10.3389/fimmu.2018.01366 (2018).
5. Centers for Disease Control and Prevention. Vaccination Coverage Among Adults Aged 65 and Over: United States, 2015. https://www.cdc.gov/nchs/products/databriefs/db281.htm
6. Abghari, P. F., Poowuttikul, P. & Secord, E. Pneumococcal Antibody Titers: A Comparison of Patients Receiving Intravenous Immunoglobulin Versus Subcutaneous Immunoglobulin. Global pediatric health 4, 2333794x16689639, doi:10.1177/2333794x16689639 (2017).

This research was funded by ADMA Biologics. The authors have no other financial or affiliations to disclose.