Session: 278. Vaccines: Influenza
Saturday, October 5, 2019. 12:15 PM

Background: Human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) are important causes of upper and lower respiratory tract infections, particularly in young children. Despite their public health impact, no effective therapeutic or preventive options are available. mRNA-1653 is a mRNA-based investigational combination vaccine against hMPV and PIV3, and consists of two distinct mRNA sequences encoding the fusion proteins of hMPV and PIV3, co-formulated in lipid nanoparticles.

Methods: This phase 1, first-in-human, randomized, placebo-controlled, dose-ranging study assesses the safety and immunogenicity of mRNA-1653 in healthy adults aged 18–49. The 124-subject study evaluates four vaccine dose levels (25, 75, 200, and 300 μg) administered intramuscularly in either single-dose or two-dose (Day 1, Month 1) vaccination schedules, with follow-up for 1 year after the last vaccination. Objectives include safety and immunogenicity measured by hMPV- and PIV3-specific neutralizing antibody titers.

Results: An interim analysis demonstrated that the mRNA-1653 vaccine was generally well-tolerated at all dose levels. Neutralizing antibodies against hMPV and PIV3 were present at baseline in all subjects, consistent with prior exposure to both viruses. A single dose of mRNA-1653 boosted serum neutralization titers against both hMPV and PIV3, and the magnitude of the response was dose-dependent across all dose levels. The geometric mean ratio of Month 1 to baseline titers was approximately 6 for hMPV and 3 for PIV3. A second dose of mRNA-1653 at Month 1 was not associated with further increase of hMPV or PIV3 neutralization titers.

Conclusions: mRNA-1653 was well-tolerated and induces a functional immune response, and is therefore a promising vaccine candidate for the prevention of pediatric respiratory tract diseases caused by hMPV and PIV3.

Disclosures. All authors: No reported disclosures.

2755. Phase 1/2, First-in-Human Study of the Safety, Tolerability, and Immunogenicity of an RSV Prefusion F-Based Subunit Vaccine Candidate

Beate Schneele-Thoma, MD, A. Davis, PhD, Kyriaki Kakarouni, MD, PhD; William C. Gruber, MD; Kariann M. Jensen, MD; Daniel Radley, MSc; Michelle S. Shaw, PhD; Joyce S. Myers, PhD; Kanggui Sun, PhD; K. Prasad; John G. Schiller, PhD; Heather Shaw, BS; Conor Smullen, PhD; Joyce S. Myers, PhD

Poster Abstracts

Session: 278. Vaccines: Influenza
Saturday, October 5, 2019. 12:15 PM

Background: The respiratory syncytial virus (RSV) fusion glycoprotein (F) is a molecule that fuses the viral and host cell membranes during virus entry as it rearranges from a meta-stable prefusion to a stable postfusion conformation. Using structural and computational design, Pfizer engineered prefusion RSV F subunit vaccine antigens with stable and well-characterized conformational homogeneity.

Methods: We report results of a 1,182 subject, first-in-human, phase 1/2, placebo-controlled, randomized, observer-blinded, dose-finding study to describe the safety, tolerability, and immunogenicity of the Pfizer RSV vaccine candidate in healthy men and non-pregnant women from 18 to 85 years of age. The study compares three doses of the vaccine candidate, with and without aluminum hydroxide, and also compares immunization with the RSV vaccine candidate alone or concomitantly with influenza vaccine. The study is ongoing to collect antibody persistence and additional safety data.

Results: The data, which are currently available for the 18- to 49-year-old subgroup, demonstrate an excellent safety and tolerability profile. Immunization with the various formulations of the vaccine candidate elicited RSV 50% neutralization titer geometric mean fold rises (GMFRs) of 10.5-17.2 for subgroup A and 10.4-19.8 for subgroup B, measured one month after immunization, with evidence of a dose-response.

Conclusion: The 10- to 20-fold increases in neutralizing antibody titers elicited by this vaccine with a stable prefusion F antigen represent a step change relative to the historical performance of vaccine candidates, such as Wyeth’s PFP, with F antigens that were not stabilized in the prefusion configuration (Simoes et al., Vaccine 20:954–60, 2002). The data strongly support development of this vaccine candidate to prevent RSV disease in infants, by immunizing pregnant women, and to prevent RSV disease in older adults, by direct immunization.

Disclosures. All authors: No reported disclosures.

2756. Pragmatic Assessment of Influenza Vaccine Effectiveness in the DoD (PAIVED), Influenza-Like Illnesses (ILI) Sub-Study at the Marine Corps Recruit Depot San Diego, CA (MCRD-SD) During the 2018–2019 Influenza Season

Ryan Marve, MD, MS,1,2,3 Gregory Otz, MD, MS,4,5 Stephanie Richard, PhD, MS,4,5 Melissa Smith, BS,2,3 Limonne Collins, MD, MPH1,2,3,4,5 Christopher Myers, PhD,6 Paul Graf, PhD,7 Rhonda Colombo, MD, MPH6,7,11,12,13 Anuradha Ganesan, MBBS, MPH8,9,10 Casey Geaney, MD8,9 Tahayaty Lalanii, MBBS2,3,14 Ana E. Markelz, MD8,9,10 Katerina Mende, PhD2,6,7,8,9,10,12,13,14 Srijith Seshadri, MBBS, MPH2,3,10 Cristina Spooner, MS1,2,3,4,5 Tyler Warkentien, MD, MPH2,3,10 Christian L. Coles, PhD2,6,7,8,9,10,12,13 Timothy Burgess, MD, MPH11,12 Naval Medical Center San Diego, San Diego, California, Infectious Disease Medical Research Program, Bethesda, Maryland, Infectious Disease Clinical Research Program, San Diego, California; Naval Medical Center San Diego, Infectious Disease Clinical Research Program, Bethesda, Maryland.