Session: P-60. New Vaccines

Background. MenACYW-TT (MenQuadfi®, Sanofi) is a quadrivalent (serogroups A, C, W, and Y) meningococcal tetanus toxoid conjugate vaccine. It was recently approved for use in persons aged ≥ 2 years in the US and persons aged ≥ 1 year in Europe and certain other countries; trials in infants as young as 6 weeks are ongoing. This study evaluated seroresponse after a MenACYW-TT booster given to adults who received either quadrivalent meningococcal polysaccharide vaccine (MSPV4) or MenACYW-TT three years earlier at age ≥ 56 years. Immune persistence up to 7 years after primary vaccination was also evaluated.

Methods. This was a Phase 3 randomized, open-label study (NCT04142242) of adults aged ≥ 59 years who participated in previous studies of MenACYW-TT vs MPSV4 (NCT01732627 and NCT02842866). The study was conducted in the US and Puerto Rico. Immune response and persistence were assessed with a serum bactericidal assay using human complement (hSBA). Sufficiency of the vaccine seroresponse was considered demonstrated if the lower limit of the 1-sided 97.5% CI for the percentage of subjects with an hSBA vaccine seroresponse against serogroups A, C, W and Y was > 40%. Safety data were collected up to 30 days after booster vaccination.

Results. A total of 471 persons were enrolled. Sufficiency of a MenACYW-TT booster was demonstrated for MPSV4- and for MenACYW-TT-primed subjects. hSBA seroresponse rates were higher among MenACYW-TT- vs MPSV4-primed subjects (79.3%–93.1% vs 49.2%–60.8%, respectively). Three to 7 years after primary vaccination, hSBA geometric mean titers (GMTs) and seroprotection rates (SPRs) declined in both MenACYW-TT- and MPSV4-primed subjects, with hSBA GMTs and SPRs for serogroups C, W, and Y generally remaining higher for MenACYW-TT- vs MPSV4-primed subjects; those for serogroup A were similar regardless of priming vaccine. Rates of adverse events following a MenACYW-TT booster were similar between MenACYW-TT- and MPSV4-primed subjects. No safety concerns were identified.

Conclusion. A MenACYW-TT booster was well tolerated and immunogenic when administered to either MPSV4- or MenACYW-primed adults aged ≥ 59 years. Up to 7 years after primary vaccination, immune persistence for serogroups C, W, and Y tended to be greater for MenACYW-TT vs MPSV4.

Disclosures. **Corwin A. Robertson, MD, MPH, FACP**, **Sanofi Pasteur** (Employee, Other Financial or Material Support, Stockholder) **Alexandre Selmani, PhD**, **Sanofi Pasteur** (Employee) **Katherine Galarza, MD**, **Sanofi Pasteur** (Employee) **Philipp Oster, MD**, **Sanofi Pasteur** (Employee, Stockholder)

1047. Development of a Next Generation 30^{+} Valent Pneumococcal Conjugate Vaccine (VAX-XP) Using Site-Specific Carrier Protein Conjugation

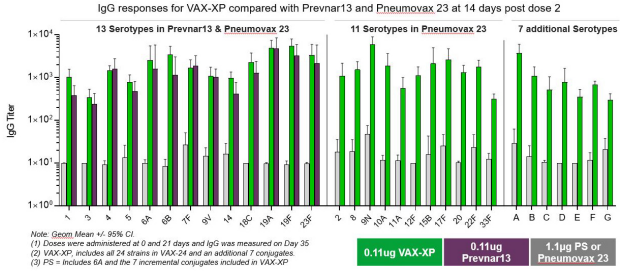
Chris Behrens, PhD[1]; Jeff Fairman, PhD[1]; Paresh Agarwal, PhD[1]; Shylaja Arulkumar, MS[1]; Sandrine Barbanel, MS[1]; Leslie Bautista, n/a[1]; Aym Berges, PhD[1]; John Burky, BS[1]; Peter Davey, MS[1]; Chris Grainger, PhD[1]; Sherry Guo, PhD[1]; Sam Iki, MS[1]; Mark Iverson, BS[1]; Neeraj Kapoor, PhD[1]; Olivier Marcq, PhD[1]; Thi-Sau Migone, PhD[1]; Lucy Pill, MS[1]; Mohammed Sardar, n/a[1]; Paul Sauer, MBA[1]; James Wassil, MS MBA[1]; [1]Vaxcyte, Inc, Foster City, California

Session: P-60. New Vaccines

Background. Due to the diversity of serotypes, exacerbated by the phenomenon of serotype replacement, there remains an unmet medical need for a pneumococcal conjugate vaccine (PCV) containing additional serotypes. Using a cell-free protein synthesis (CFPS) platform to produce an enhanced carrier protein (eCRM®) based on the CRM_{197} sequence, Vaxcyte is developing a PCV encompassing over 30 serotypes. The eCRM carrier protein contains multiple insertions of the non-native amino acid para-azidomethyl-L-phenylalanine (pAMF) that facilitates site-specific conjugation of the pneumococcal polysaccharides (PS) to eCRM. Unlike conventional methodologies, site-selective conjugation enhances process consistency and increases capacity for inclusion of additional serotypes in a PCV without promoting carrier suppression. Using this platform, the aim of the current study was to employ CFPS technology to construct a 31-valent PCV and evaluate its immunogenicity in New Zealand White (NZW) rabbits.

Methods. The eCRM carrier protein was individually conjugated to each of 31 selected pneumococcal PSs using copper-free click chemistry to produce 31 Conjugate Drug Substances (DS), which were then mixed with aluminum phosphate to produce the VAX-XP Drug Product. 24 of the DS conjugates in VAX-XP were generated at manufacturing scale. Two doses of VAX-XP were administered to NZW rabbits at 0 and 21 days to assess its ability to elicit anti-capsular IgG antibodies. Additionally, rabbits were also administered either Prevnar13 or a mixture of Pneumovax 23 and 8 incremental PS in isotonic saline, as comparators.

Results. VAX-XP showed conjugate-like immune responses for all 31 serotypes, as demonstrated by superior responses to PS-based vaccines and comparable responses to Prevnar13. IgG responses for VAX-XP compared with Prevnar13 and Pneumovax 23 at 14 days post dose 2



Conclusion. These results demonstrate that increasing the number of pneumococcal serotypes does not result in immunological attenuation in any of the serotypes contained in VAX-XP relative to the current standard of care. Furthermore, the data confirm the scalability and reproducibility of the CFPS platform in the production of VAX-XP conjugates, creating the foundation for a next generation broad-valency PCV.

Disclosures. **Chris Behrens, PhD**, **Vaxcyte, Inc.** (Employee) **Jeff Fairman, PhD**, **Vaxcyte, Inc.** (Employee) **Paresh Agarwal, PhD**, **Vaxcyte, Inc.** (Employee) **Shylaja Arulkumar, MS**, **Vaxcyte, Inc.** (Employee) **Sandrine Barbanel, MS**, **Vaxcyte, Inc.** (Employee) **Leslie Bautista, n/a**, **Vaxcyte, Inc.** (Employee) **Aym Berges, PhD**, **Vaxcyte, Inc.** (Employee) **John Burky, BS**, **Vaxcyte, Inc.** (Employee) **Peter Davey, MS**, **Vaxcyte, Inc.** (Employee) **Chris Grainger, PhD**, **Vaxcyte, Inc.** (Employee) **Sherry Guo, PhD**, **Vaxcyte, Inc.** (Employee) **Sam Iki, MS**, **Vaxcyte, Inc.** (Employee) **Mark Iverson, BS**, **Vaxcyte, Inc.** (Employee) **Neeraj Kapoor, PhD**, **Vaxcyte, Inc.** (Employee) **Olivier Marcq, PhD**, **Vaxcyte, Inc.** (Employee) **Thi-Sau Migone, PhD**, **Vaxcyte, Inc.** (Employee) **Lucy Pill, MS**, **Vaxcyte, Inc.** (Employee) **Mohammed Sardar, n/a**, **Vaxcyte, Inc.** (Employee) **Paul Sauer, MBA**, **Vaxcyte, Inc.** (Employee) **James Wassil, MS MBA**, **Vaxcyte, Inc.** (Employee)

1048. Double-Blind, Randomized, Placebo-Controlled Phase 2b Multicenter Trial of V160, a Replication-Defective Human Cytomegalovirus (CMV) Vaccine

Rituparna Das, MD[1]; Daniel Blazquez-Gamero, MD[2]; David I. Bernstein, MD MA[3]; Soren Gantt, MD[4]; Oliver Bautista, PhD[1]; Karen Beck, RN, BSN[1]; Anthony Conlon, PhD[1]; Daniel Rosenbloom, PhD[1]; Dai Wang, PhD[1]; Michael Ritter, BA[1]; Beth Arnold, MS[1]; Paula Annunziato, MD[1]; Kevin Russell, MD, MTM&H[5]; [1]Merck & Co., Inc., Kenilworth, New Jersey; [2]Pediatric Infectious Diseases Unit, Hospital Universitario; [12] de Octubre and Universidad Complutense, Instituto de Investigación Hospital; [12] de Octubre (imas12) RECLIP, Madrid, Madrid, Spain; [3]Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH; [4]CHU Sainte-Justine Research Centre, Université de Montréal, Montreal, Quebec, Canada; [5]Merck and Co Inc., North Wales, PA

Session: P-60. New Vaccines

Background. Preventing congenital cytomegalovirus infection (CMVi) is an important unmet need. Natural maternal immunity to CMV acquired prior to pregnancy appears to reduce fetal transmission. In a Phase 1 trial, V160, a replication-defective CMV vaccine expressing the pentameric complex, induced humoral and cell-mediated immune (CMI) responses comparable to natural immunity.

Methods. Healthy, CMV-seronegative women aged 16–35 years were randomized 1:1:1 to receive double-blind V160 in a 3- or 2-dose regimen or placebo. Primary and secondary endpoints were efficacy in reducing the incidence of CMVi with 3-dose or 2-dose regimens of V160 vs placebo, respectively, using a fixed-event design. Monthly urine and saliva samples were collected to identify CMVi by polymerase chain reaction (PCR) with a single positive sample considered evidence of infection. Immunoglobulin G (IgG) binding to glycoprotein B (gB) and CMV-specific neutralizing antibody (NAb) were measured in all participants, and CMI responses were measured in a subset. Injection-site and systemic adverse events (AEs) were collected for 5 days and 14 days, respectively, after each vaccination and serious AEs were collected for the trial duration.

Results. 2200 women from 7 countries were enrolled (of 7458 screened). Over 80% of participants received all doses, and compliance with saliva and urine samples was > 95%. Vaccine efficacy (VE) of 42.4% (95% CI -13.5, 71.1%) was demonstrated in the 3-dose group vs placebo. In the 2-dose group, VE was -32.0% (95% CI -135.0, 25.0%). Both the quantity and duration of CMV shedding in urine and saliva among cases of CMVi decreased in the 3-dose, but not the 2-dose group vs placebo. Both V160 regimens elicited humoral and CMI responses detected by CMV-specific NAb, gB IgG, and ELISpot, which peaked at Month 7 and continued to be detectable at Month 24. Mild to moderate AEs were more frequently reported in V160 vs placebo recipients, but no vaccine-related serious AEs or deaths were reported.

Conclusion. V160 was well tolerated and immunogenic, but neither the 3-dose nor 2-dose regimen demonstrated significant efficacy against CMVi as defined in this trial. The quantity and duration of CMV shedding was reduced in the 3-dose group, suggesting V160 may improve immune control of viral replication after CMVi.

Disclosures. **Rituparna Das, MD**, **Merck & Co, Inc.** (Employee) **Daniel Blazquez-Gamero, MD**, **MSD** (Other Financial or Material Support, Fees for lectures in educational activities) **Soren Gantt, MD**, **Altona Diagnostics** (Research Grant or Support)**Merck** (Consultant, Grant/Research Support)**Meridian Biosciences** (Research Grant or Support)**Moderna** (Consultant, Research Grant or Support)**VBI Vaccines Inc** (Research Grant or Support) **Oliver Bautista, PhD**, **Merck & Co, Inc.** (Employee) **Karen Beck, RN, BSN**, **Merck & Co, Inc.** (Employee) **Anthony Conlon, PhD**, **Merck & Co, Inc.** (Employee) **Daniel Rosenbloom, PhD**, **Merck & Co, Inc.** (Employee) **Dai Wang, PhD**, **Merck & Co, Inc.** (Employee) **Michael Ritter, BA**, **Merck & Co, Inc.** (Employee) **Beth Arnold, MS**, **Merck & Co, Inc.** (Employee, Shareholder) **Paula Annunziato, MD**, **Merck & Co, Inc.** (Employee) **Kevin Russell, MD, MTM&H**, **Merck & Co., Inc.** (Employee, Shareholder)

1049. Minimal Transient HIV-1 Viremia Following Vaccination Regimens Containing AD26. ZEBOV and MVA-BN-Filo in ART-Suppressed People Living with HIV

Benjamin L. Custer, M.D.[1]; Betty Mwesigwa, MBchB, MSc Clinical Trials[2]; Fredrick Sawe, MBCHB, MMED[3]; Janet Oyieko, MD[4]; Nyanda Ntinginya, MD, MSc, PhD[5]; Ilesh Jani, MD PhD[6]; Michael Iroezindu, MB, BS[7]; Jack Hutter, MD[8]; Linda Jagodzinski, Ph.D.[9]; Georgi Shukarev, MD[10]; Leigh Anne Eller, PhD[11];