

potential opportunity for vaccination of high-risk patients in order to promote primary prevention in future waves of pandemics.

Disclosures: All Authors: No reported disclosures

12. Randomized Studies of Two Clostridioides (Clostridium) difficile Vaccine Formulations

Jody Lawrence, MD¹; Nicholas Kitchin, MD¹; Annaliesa S. Anderson, PhD²; Michael W. Pride, PhD²; Kathrin U. Jansen, PhD²; William C. Gruber, MD¹; Yahong Peng, PhD¹; Kevin Yi, PhD³; Charles Knirsch, MD³; Chris Webber, MD³; ¹Pfizer Inc, Collegetown, Pennsylvania; ²Pfizer, Pearl River, NY; ³Pfizer, Inc, Collegetown, Pennsylvania; ⁴Pfizer, Ltd. Hurley UK, Hurley, England, United Kingdom

Session: P-2. Adult Vaccines

Background: Two formulations of investigational bivalent *Clostridioides (Clostridium) difficile* vaccine (QS-21 adjuvanted toxoid and toxoid-alone) were assessed for safety and immunogenicity in randomized studies in healthy adults 50–85 years of age.

Methods: The Phase 1 study of QS-21 adjuvanted toxoid vaccine randomized subjects 3:1 to 100 µg QS-21-containing *C. difficile* vaccine or placebo; 3 doses were given according to 2 different schedules: a shortened month (Months 0, 1, 3) or day (Days 1, 8, 30) regimen. The Phase 2 toxoid-alone vaccine study randomized subjects 3:3:1 to receive 100 or 200 µg unadjuvanted *C. difficile* vaccine formulation or placebo in Stages 1 and 2 (sentinel cohorts of different age groups), and 3:1 to receive the selected dose of unadjuvanted *C. difficile* vaccine formulation or placebo in Stage 3. Three doses were given on a day (Days 1, 8, 30) regimen. Safety was the primary outcome for both studies. Immunogenicity was determined by measuring serum toxin A- and B-specific neutralizing antibodies.

Results: In the day regimen, 10 reports across both studies of grade 3 injection site redness postdose 2 triggered predefined stopping rules. Local reactions in both studies were more common among vaccine versus placebo recipients. Injection site pain predominated and was generally mild in severity. Systemic events were infrequent and generally mild-to-moderate in severity. Adverse events were reported by 50.0%–75.0% and 16.7%–50.0% of subjects in the QS-21 and toxoid-alone studies, respectively. Immune responses peaked around Day 37 (shortened-month regimen) or between Day 15 and Month 2 (day regimen), and remained above baseline throughout follow-up.

Conclusion: Both formulations demonstrated robust immunogenicity. However, both studies stopped early due to grade 3 injection site redness postdose 2 of the day (Days 1, 8, 30) regimen; neither formulation progressed to later stage development. Instead, an aluminum hydroxide-containing formulation of the vaccine candidate administered at 0, 1, and 6 months, which was safe and immunogenic in phase 1 and 2 studies, advanced to phase 3 studies.

Disclosures: Jody Lawrence, MD, Pfizer, Inc (Employee) Nicholas Kitchin, MD, Pfizer, Inc (Employee) Annaliesa S. Anderson, PhD, Pfizer (Employee, Shareholder) Michael W. Pride, PhD, Pfizer (Employee, Shareholder) Kathrin U. Jansen, PhD, Pfizer (Employee, Shareholder) William C. Gruber, MD, Pfizer (Employee, Shareholder) Yahong Peng, PhD, Pfizer (Employee, Shareholder) Charles Knirsch, MD, Pfizer (Employee) Chris Webber, MD, Pfizer Inc (Employee, Shareholder)

13. Uncommon rash and neurological symptoms related to Shingrix

sanjay K. Yadava, MD¹; Rahul Mahapatra, DO²; ¹SUNY upstate medical university, Syracuse, New York ²SUNY Upstate Medical University, Syracuse, New York

Session: P-2. Adult Vaccines

Background: Shingrix is a non-live recombinant vaccine approved by the Food and Drug Administration (FDA) in 2017 to prevent shingles and postherpetic neuralgia in immunocompetent adults age 50 years and older. A myriads of local and systemic reactions due to the vaccine have been reported, but diffuse erythematous maculopapular rash and neurological symptoms have not yet been reported in English literature.

Methods: Using Google and PubMed, we searched for relevant case reports and journal articles describing adverse effects related to shingrix vaccination.

Results: A 54-year female without significant past medical history presented with diffuse erythematous maculopapular rash, itching and a feeling of weakness in both legs. Her symptoms started with itching and erythematous macular rash at the site of shingles shot followed by headache, myalgia, and malaise which did not improved much with Benadryl. Next day, she felt numbness and weakness in both legs. On the third day, she awoke with diffuse red rash on the face, trunk, lower extremities, fewer lesions on upper extremities. Her review of systems was negative except as mentioned. On examination, she was found to have diffuse erythematous maculopapular itchy rash as shown in Fig 1, but no sensory, motor, cranial nerve or cerebellar signs. Infectious disease was consulted who recommended IV acyclovir considering early varicella with given morphology. The morphology of lesions did not change over a period of times and VZV PCR of lesions came negative hence acyclovir was discontinued after three days. Her symptoms and rash improved over the hospital stay with supportive treatment and was discharged home on day fifth of admission.

Fig. 1A, Rash over face



Fig. 1B, Rash over right thigh



Conclusion: The safety of shingrix was evaluated by the pool data from eight clinical trials of more than 10,000 participants. Among the study population, 9.4% had local injection-site reactions including pain, redness, and swelling and 10.8% had systemic events including myalgia, fatigue, headache, shivering, fever, and gastrointestinal symptoms. The nature and duration of rash described in our patient has not been reported in english literature including these clinical trials. Noticing new reactions with broad use of new vaccine is conceivable.

Disclosures: All Authors: No reported disclosures

14. A Comprehensive Real-World Analysis to Compare Adjuvanted Trivalent Influenza Vaccine and Trivalent High Dose Influenza Vaccine by Age and Period of High Influenza Activity for the 2018–19 Season among U.S. Elderly

Maarten Postma, Dr.¹; Stephen I. Pelton, MD²; Victoria Divino, PhD³; Joaquin F. Mould-Quevedo, PhD⁴; Drishti Shah, PhD³; Mitchell DeKoven, PhD³; ¹University of Groningen, Groningen, Groningen, Netherlands; ²Boston Medical Center, Boston, Massachusetts; ³IQVIA, Falls Church, Virginia; ⁴Seqirus Vaccines Ltd., Summit, New Jersey

Session: P-2. Adult Vaccines

Background: Influenza vaccine effectiveness decreases with increasing age due to the senescence of immune function and a reduced immune response to antigens. There is also considerable vaccine effectiveness heterogeneity depending on the influenza activity time period, especially in seasons where two different circulating strains predominated, such as the 2018–19 season. This research aimed to assess the effect of age and high influenza activity period (HIAP) on the relative vaccine effectiveness (rVE) of adjuvanted trivalent influenza vaccine (aTIV) vs. trivalent high-dose influenza vaccine (HD-TIV) among elderly (≥65y) recipients in the U.S.

Methods: During the 2018–19 influenza season, a retrospective cohort analysis was conducted using professional fee, prescription claims and hospital charge master data in the U.S. The first sub-analysis evaluated rVE for different age groups (65–74 years, 75–84 years, ≥85 years). The second sub-analysis evaluated rVE overall, restricting the observation period from to HAIP: Dec 2018–Mar 2019 (August 2018–July 2019 in the main analysis). Adjusted analyses were conducted through inverse probability of treatment weighting (IPTW) to control for selection bias. Poisson regression was used to estimate the adjusted pairwise rVE for influenza-related hospitalizations/emergency room (ER) visits and office visits.

Results: Following IPTW, 561,315 recipients of aTIV and 1,672,779 of TIV-HD were identified. Following IPTW adjustment and Poisson regression, aTIV was more effective in reducing influenza-related office visits compared to TIV-HD (7.0%; 95% CI: 2.6%–11.2%) in the HIAP sub-analysis. In the age sub-analysis, the rVE favoring aTIV ranged from 5.1% (95% CI: -0.17%–10.1%) for the youngest group (65–74) up to 11.4% (95% CI: 0.6%–21.1%) for the eldest group (≥85y) for influenza-related office visits. No

statistically significant differences were found for aTIV compared to TIV-HD for prevention of influenza-related hospitalizations/ER visits in the sub-analyses evaluated.

Conclusion: In adjusted analyses, aTIV reduced influenza-related office visits compared to TIV-HD within the two older age groups and HIAP sub-analysis. aTIV and TIV-HD demonstrated comparable reductions in influenza-related hospitalizations/ER visits.

Disclosures: Maarten Postma, Dr., IQVIA (Consultant) Stephen I. Pelton, MD, Merck vaccine (Consultant, Grant/Research Support)Pfizer (Consultant, Grant/Research Support)Sanofi Pasteur (Consultant, Other Financial or Material Support, DSMB)Seqirus Vaccine Ltd. (Consultant) Victoria Divino, PhD, Seqirus Vaccines Ltd. (Consultant) Joaquin E. Mould-Quevedo, PhD, Seqirus Vaccines Ltd. (Employee, Shareholder) Drishti Shah, PhD, Seqirus Vaccines Ltd. (Consultant) Mitchell DeKoven, PhD, Seqirus Vaccines Ltd. (Consultant)

15. A Novel Approach to Bacterial Vaccines: Haemophilus influenzae as a Paradigm

Terrence Stull, MD¹; Paul Whitby, PhD¹; Daniel Morton, PhD²; Huda Mussa, PhD¹; Lucia Mirea, PhD¹; ¹University of Arizona College of Medicine-Phoenix, PHOENIX, Arizona; ²University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

Session: P-2. Adult Vaccines

Background: The *H. influenzae* type b vaccines target the type b capsule and therefore have no impact on the nontypable (unencapsulated) *H. influenzae* (NTHi). NTHi has become the most common cause of otitis media and is the most common isolate from patients with exacerbations of Chronic Obstructive Pulmonary Disease (COPD). Therefore, NTHi is an appropriate target for vaccine development.

Methods: To characterize potential vaccine targets, the core outer proteins of NTHi present in the available sequenced genomes were identified through genomic bioinformatics. The structures of the outer proteins were analyzed through comparison with the available structures of homologues characterized by X-ray crystallography. Sequenced conserved outer regions of these proteins were analyzed for their protective capacity in the infant rat model of *H. influenzae* infection.

Results: Nine peptides that were protective in the infant rat model were used in a novel vaccine to immunize chinchillas, the most established animal model of otitis media. Chinchillas (40 vaccinated and 41 controls) were infected with NTHi 86-028NP. The vaccinated group cleared infection more quickly than the control group as indicated by significantly decreased positive findings on video-otoscopy ($p < 0.0001$) and tympanometry ($p = 0.0002$) on day 7, and presence of middle ear fluid obtained by aspiration ($p = 0.0001$) on day 10 post infection. Similarly, in the mouse model of NTHi pulmonary clearance, the vaccinated group ($n = 5$) reduced infection more rapidly than the control group ($n = 5$), $p = 0.008$.

Conclusion: These data demonstrate the effectiveness of the Bacterial Vaccine Polypeptide methodology in development of a vaccine against NTHi with protection in relevant preclinical models of both otitis media and pulmonary clearance. The methods are applicable to other bacteria, and this approach to a Bacterial Vaccine Polypeptide against NTHi serves as a paradigm for development of similar vaccines to protect against other bacterial infections.

Disclosures: All Authors: No reported disclosures

16. A Randomized Phase 1 Study of a Novel Pneumococcal Conjugate Vaccine in Healthy Japanese Adults in the United States

David Fitz-Patrick, MD¹; Mariano Young Jr., MD²; Daniel Scott, MD³; Ingrid L. Scully, PhD⁴; Gary Baugher, PharmD²; Yahong Peng, PhD²; Kathrin U. Jansen, PhD³; William C. Gruber, MD³; Wendy Watson, MD⁴; ¹East-West Medical Institute, Honolulu, Hawaii; ²Pfizer Inc, Collegeville, Pennsylvania; ³Pfizer, Collegeville, Pennsylvania; ⁴Pfizer Vaccine Research and Development, Pearl River, New York

Session: P-2. Adult Vaccines

Background: Because of the number and variability of serotypes causing pneumococcal disease among different geographic regions, age groups, and environmental backgrounds, expanding serotype coverage with pneumococcal conjugate vaccines (PCVs) is a continued unmet need.

Methods: This phase 1, randomized, double-blind study included healthy Japanese adults aged 18–49 years residing in the United States. Subjects were randomized 1:1:1 to receive a single dose of a 20-valent PCV (containing 13-valent PCV [PCV13] serotypes plus 8, 10A, 11A, 12F, 15B, 22F, 33F), a novel pneumococcal polysaccharide conjugate vaccine with extended coverage, or PCV13 (control). Safety was the primary endpoint and included reactogenicity events occurring ≤ 14 days after vaccination, adverse events (AEs) ≤ 1 month after vaccination, and serious AEs (SAEs) ≤ 6 months after vaccination. The secondary endpoint was pneumococcal serotype-specific immunogenicity as determined by opsonophagocytic activity (OPA) titers on sera collected before and 1 month after vaccination.

Results: Overall, 35 subjects received PCV20 and 35 subjects received PCV13. One subject withdrew before the 1-month follow-up. Local reactions and systemic events across groups were generally mild or moderate (Figure 1). Two vaccine-related AEs occurred (injection site erythema and swelling in the PCV20 group); no severe AEs, SAEs, or safety-related withdrawals were reported. OPA geometric mean titers increased for all 20 serotypes in the PCV20 group and all 13 serotypes in the PCV13 group 1 month after vaccination; corresponding OPA geometric mean fold rises from baseline to 1 month after vaccination are reported (Figure 2; Figure 3).

Figure 1

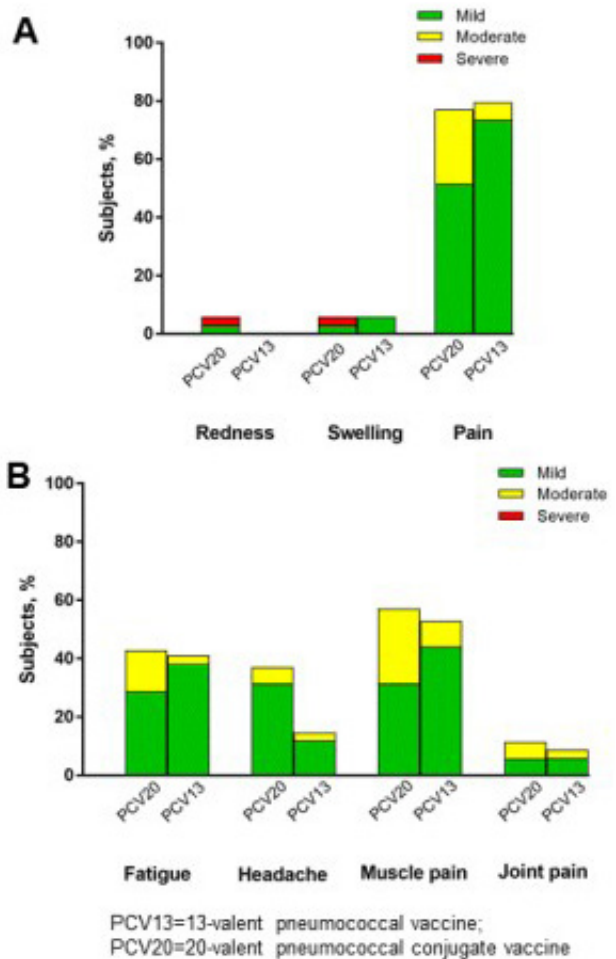
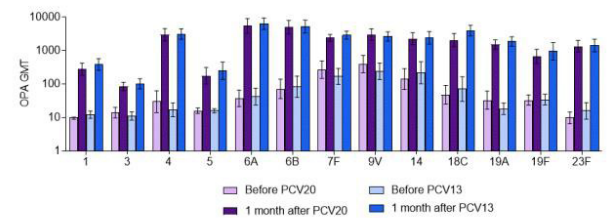


Figure 2



Serotype	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F
PCV20	GMFR	29.1	6.1	96.3	11.0	144.7	65.0	8.4	7.5	11.9	38.8	46.3	20.3
	95% CI	18.9	4.4	40.5	6.0	70.7	31.4	4.4	4.3	5.8	19.1	24.3	11.6
		44.8	8.5	228.9	20.0	296.4	134.2	15.8	13.1	24.3	78.8	88.3	35.7
PCV13	GMFR	31.8	9.2	177.6	15.7	152.7	46.7	18.1	11.3	11.2	53.7	98.9	27.4
	95% CI	21.4	6.4	97.6	8.5	77.0	22.2	10.6	6.8	5.1	24.0	60.4	14.5
		47.2	13.3	323.3	28.7	302.6	98.2	30.8	18.9	24.5	120.0	162.1	51.6

GMFR=geometric mean fold rise; GMT=geometric mean titer; LLOQ=lower limit of quantitation; OPA=opsonophagocytic activity; PCV13=13-valent pneumococcal conjugate vaccine; PCV20=20-valent pneumococcal conjugate vaccine. Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.