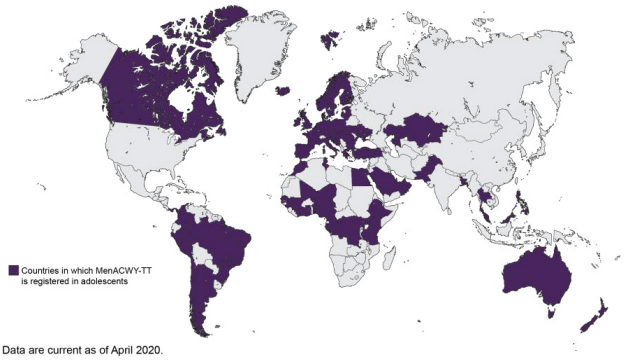
Figure 1. Global Registration Status of MenACWY-TT (Nimenrix®) in Adolescents



Data are current as of April 2020.

Table 1. Pivotal Clinical Studies of MenACWY-TT (Nimenrix®) Supporting Licensure in Adolescents

Phase	Type (identifier)	Design	Subjects		Immunogenicity, %[f] (rSBA titer ≥ 1:8)		Location
			Age, y	n[a]	MenACWY-TT	MenACWY-DT/PS	
2	Primary (NCT01165242)	MenACWY-TT vs MenACWY-DT	10–25	1011	51.0–82.5[g]	39.0–76.3[g]	United States, Canada
	Extension (NCT00715910)	Antibody persistence ≤ 5 y postprimary		312[b]	48.9–94.4	44.4–90.9	United States
2	Primary (NCT00356369)	MenACWY-TT vs MenACWY-PS	11–17[c]	301	99.6–100	100	Saudi Arabia, Philippines
	Extension (NCT00356369	Antibody persistence ≤ 5 y postprimary		284	74.0–92.8	23.7–80.3	Saudi Arabia, Philippines
	Extension (NCT01934140)	Antibody persistence ≤ 10 y postprimary; MenACWY-TT booster		182[d,e]	69.3–91.2; 100	24.4–88.9; 97.7–100	Philippines
3	Primary (NCT00464815)	MenACWY-TT vs MenACWY-PS	11–17	1025	99.7–100	99.6–100	India, Philippines, Taiwan
	Extension (NCT00974363)	Antibody persistence 5 y postprimary		478	86.0–97.5	34.9–93.0	India, Philippines
	Extension (EudraCT 2013-001512-29)	Antibody persistence ≤ 10 y postprimary; MenACWY-TT booster		229	71.6–90.7; 100	43.1–82.4; 98.0–100	Philippines

MenACWY-D=quadrivalent meningococcal vaccine conjugated to diptheria toxin; MenACWY-PS=quadrivalent meningococcal polysaccharide vaccine; MenACWY-TT=quadrivalent meningococcal vaccine conjugated to tetanus toxoid.
[a]The number of subjects who received vaccination unless otherwise specified.
[b]The number of subjects with the longest follow-up period.
[c]Study included subjects aged 11–55 y, but only data for those aged 11–17 y are presented.
[d]Values at year 10 are shown.
[e]207 subjects had immunogenicity assessments for 1 mo postbooster.
[f]Percentage of subjects.
[g]Vaccine response was defined as a serum bactericidal titer of ≥ 1:8 in subjects initially seronegative (titer < 1:4) and as a 4-fold increase in titer in subjects initially seropositive (titer ≥ 1:4).

Methods: Immunogenicity and safety data from these 8 clinical studies are summarized.

Results: Across studies, MenACWY-TT antibody responses against all vaccine serogroups were comparable to those of other MenACWY vaccines 1 month post vaccination (**Table 1**). Antibody responses to MenACWY-TT persisted for up to 10 years in those vaccinated during adolescence. A MenACWY-TT booster given 10 years after primary meningococcal vaccination in early childhood or adolescence elicited robust antibody responses. MenACWY-TT had an acceptable safety profile, with reactogenicity events most commonly reported. Reactogenicity profiles with MenACWY-TT booster were similar to those seen after primary MenACWY-TT.

Conclusion: The MenACWY-TT clinical study program demonstrated the immunogenicity and safety of primary and booster dosing in adolescents. Immune responses persisted through 10 years after primary vaccination.

Funding: Pfizer.

Disclosures: Paula Peyrani, MD, Pfizer Inc (Employee, Shareholder) Chris Webber, MD, Pfizer Inc (Employee, Shareholder) Cindy Burman, PharmD, Pfizer Inc (Employee, Shareholder) Paul Balmer, PhD, Pfizer Inc (Employee, Shareholder) John L. Perez, MD, MA, Pfizer Inc (Employee, Shareholder)

4. MenACWY-TT Long-Term Antibody Persistence Following Adolescent Vaccination and Evaluation of a Booster Dose: A Review of Clinical Data

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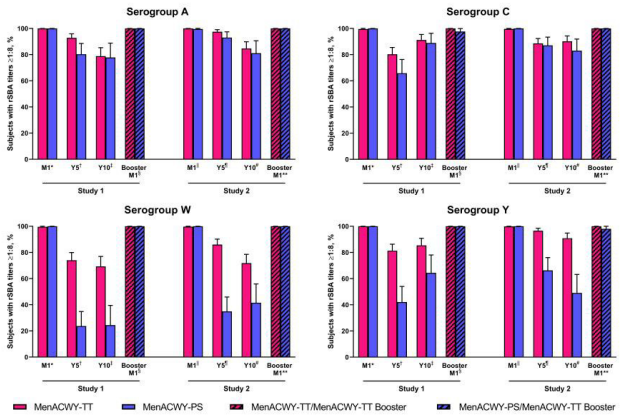
Session: P-1. Adolescent Vaccines

Background: A peak in meningococcal carriage and invasive meningococcal disease (IMD) occurs during adolescence and young adulthood. In the United States, preventive vaccination with a quadrivalent meningococcal (MenACWY) conjugate vaccine is recommended at age 11–12 years, with a booster dose given at age 16 years. MenACWY-TT (Nimenrix®), a MenACWY tetanus toxoid conjugate vaccine, was first licensed in 2012 and is available in the European Union and 50 other countries. Immune responses to other MenACWY conjugate vaccines decline over several years following vaccination. Here, we review 2 recent studies evaluating the long-term persistence of MenACWY-TT immune responses in adolescents as well as safety and immunogenicity of a booster dose given 10 years after primary vaccination.

Methods: Both studies (ClinicalTrials.gov NCT01934140, NCT03189745) were extensions of phase 2 or 3 studies of subjects 11–17 years of age given a single dose of MenACWY-TT or MenACWY polysaccharide vaccine (MenACWY-PS). Immune responses through 10 years after primary vaccination and after a Year 10 MenACWY-TT booster dose were measured by serum bactericidal antibody assays using baby rabbit complement (rSBA). Specific endpoints included percentages of subjects with rSBA titers ≥1:8 and ≥1:128 and geometric mean titers (GMTs). Booster dose safety and tolerability were also evaluated.

Results: In both studies, the percentages of subjects with rSBA titers ≥1:8 through 10 years postvaccination were generally higher or similar among MenACWY-TT (69.3%–91.2% at Year 10; n=137–163) compared with MenACWY-PS (24.4%–88.9%; n=45–53) recipients for all 4 serogroups (**Figure**); similar results were observed for GMTs (146.0–446.9 vs 12.9–191.0 at Year 10). One month after a MenACWY-TT booster dose, 97.7%–100% of subjects across groups had titers ≥1:8 (**Figure**), and GMTs were markedly higher than prebooster values. No new safety signals were identified following the booster dose.

Figure 1. Subjects in each of the 2 studies with rSBA titers ≥1:8 before and at 1 month, 5 years, and 10 years after primary vaccination with MenACWY-TT or MenACWY-PS at 11–17 years of age and 1 month after booster vaccination with MenACWY-TT at 10 years following primary vaccination.



95% CIs are indicated by error bars.
*MenACWY-TT, n=214–224; MenACWY-PS, n=74–76; [†]MenACWY-TT, n=208; MenACWY-PS, n=76; [‡]MenACWY-TT, n=137; MenACWY-PS, n=45; [§]MenACWY-TT, n=133; MenACWY-PS, n=44; [‖]MenACWY-TT, n=752–759; MenACWY-PS, n=252; [¶]MenACWY-TT, n=236; MenACWY-PS, n=85–86; [#]MenACWY-TT, n=163; MenACWY-PS, n=53; **MenACWY-TT, n=162; MenACWY-PS, n=51.
MenACWY-PS=quadrivalent meningococcal polysaccharide vaccine; MenACWY-TT=quadrivalent meningococcal tetanus toxoid conjugate vaccine; rSBA=serum bactericidal antibody assay using baby rabbit complement.

Conclusion: Functional antibodies for all 4 serogroups persisted through 10 years after MenACWY-TT adolescent vaccination, suggesting that this vaccine may help prevent IMD throughout the lengthy risk period in this group. A MenACWY-TT booster dose may further extend protection regardless of the primary vaccine received.

Funded by Pfizer.

Disclosures: Paula Peyrani, MD, Pfizer Inc (Employee, Shareholder) Chris Webber, MD, Pfizer Inc (Employee, Shareholder) Cindy Burman, PharmD, Pfizer Inc (Employee, Shareholder) Paul Balmer, PhD, Pfizer Inc (Employee, Shareholder) John L. Perez, MD, MA, Pfizer Inc (Employee, Shareholder)

5. Observational Study of Routine Use of 9-Valent Human Papillomavirus Vaccine: Safe in More Than 140,000 Individuals

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Session: P-1. Adolescent Vaccines

Background: Nine-valent human papillomavirus (HPV) vaccine (9vHPV vaccine, Gardasil®9) was licensed in the US in Dec-2014. Using a self-controlled risk interval design, we conducted a post-licensure retrospective cohort study within Kaiser Permanente in Northern California (KPNC) to assess 9vHPV safety following routine administration.

Methods: We included KPNC members 9-years or older who received 9vHPV as their first dose of HPV vaccine between Oct-2015 and Sep-2017. Post-vaccination emergency and hospitalization events were compared during risk intervals (days 1–60 and 0–14) with later self-comparison intervals using conditional logistic regression, following all 9vHPV vaccine doses combined, and by dose. We investigated significant

findings by assessing post-vaccination timing and medical record reviews. We evaluated and reviewed medical records for all day 0 allergic reaction and syncope events, and all deaths during the study. An independent Safety Review Committee reviewed potential safety signals.

Results: We studied 140,628 9vHPV-vaccinated individuals, including 69,027 (49%) who received 2 doses and 29,901 (21%) 3 doses, totaling 239,556 doses. Eight categories were significantly increased in at least one analysis (Table). On review, most findings were previously known, preceded vaccination, or were better explained by other medical history. Some day 0 allergic reactions and syncope were potentially related to vaccination. None of the 20 deaths were considered related to 9vHPV.

Table. Elevated diagnosis categories comparing risk and self-comparison intervals.

Diagnosis Categories	ORs (95% CI)
Diabetes mellitus	1.66 (1.01, 2.74)
Delirium	NE (1.11, NE)
Nervous system disorders^{+2}	1.33 (1.02, 1.72)
Digestive disorders^{+4}	1.21 (1.03, 1.41)
Male genital disease	1.60 (1.04, 2.46)
Skin disorders^{+1}	1.88 (1.00, 3.53)
Congenital anomalies, nervous system	5.01 (1.10, 22.83)
Symptoms, ill-defined^{+1}	1.36 (1.13, 1.64)

$^{+n}$ indicates number of elevated sub-categories, for a total of 16 categories. NE: not estimable.

Conclusion: This large study of individuals who received only 9vHPV vaccine did not identify any new safety events related to 9vHPV administration and provides reassuring evidence of the favorable safety profile of the 9vHPV vaccine.

Disclosures: Se Li, PhD, Merck & Co., Inc. (Employee, Shareholder) Christine Velicer, PhD, Merck & Co., Inc. (Employee, Shareholder) Patricia Saddier, MD, PhD, Merck & Co., Inc. (Employee, Shareholder) Nicola P. Klein, MD, PhD, GSK group of companies (Research Grant or Support)Merck (Grant/Research Support)Pfizer (Grant/Research Support)Protein Science (now SP) (Grant/Research Support)Sanofi Pasteur (Grant/Research Support)

6. Pentavalent Meningococcal (MenABCWY) Vaccine is Safe and Well Tolerated With Immunogenicity Noninferior to Coadministered MenB-FHbp and MenACWY-CRM in a Phase 2 Study of Healthy Adolescents and Young Adults

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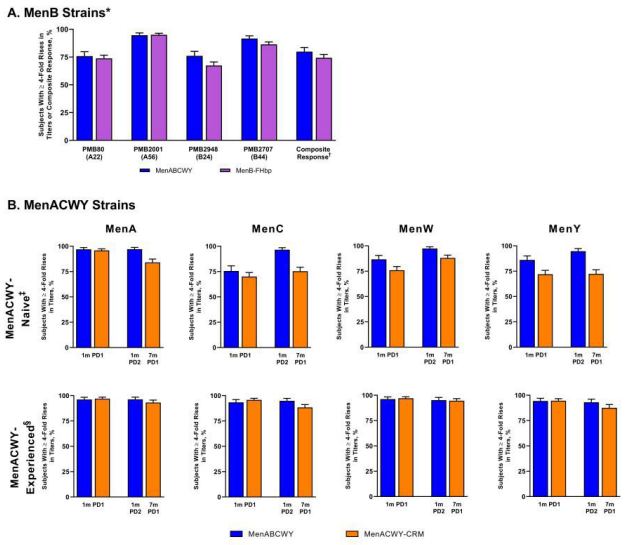
Session: P-1. Adolescent Vaccines

Background: Meningococcal serogroups A, B, C, W and Y cause nearly all meningococcal disease globally. Vaccination is complicated by different dosing recommendations for serogroup B (MenB) and quadrivalent (MenACWY) vaccines, which could be solved with a single pentavalent vaccine. This study in adolescents and young adults evaluated a new pentavalent MenABCWY vaccine that combines 2 licensed vaccines, MenB-FHbp (Trumenba®; bivalent rLP2086) and MenACWY-TT (Nimenrix®), into a single vaccine.

Methods: In this ongoing, randomized, controlled, observer-blinded, multicenter study (NCT03135834), MenB vaccine-naive and MenACWY-naive or -experienced healthy 10–25-year-olds were randomized 1:2 to MenABCWY (Month 0,6) or MenB-FHbp (Month 0,6) and MenACWY-CRM (Month 0). Immune responses were measured by serum bactericidal activity assays with human complement (hSBA) against serogroup A, C, W and Y strains and 4 diverse, vaccine-heterologous MenB strains. Endpoints included percentages of subjects achieving ≥ 4-fold rises in titers from baseline. Noninferiority of immune responses was assessed at the 10% margin (95% CI lower limit > −10%). Safety was assessed.

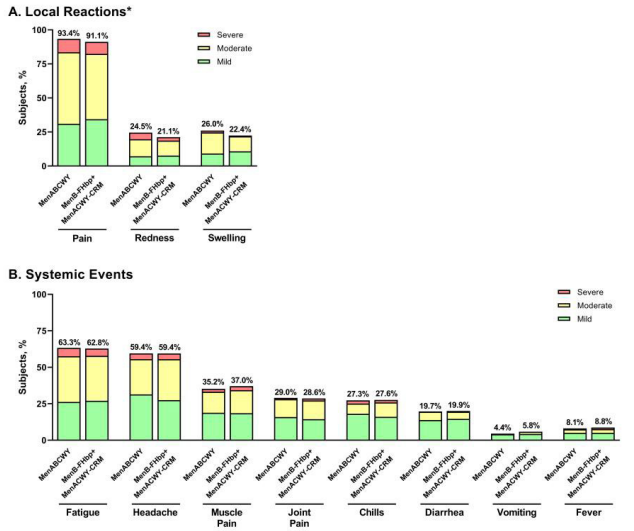
Results: Following dose 2, high percentages of MenABCWY (n=543) and MenB-FHbp (n=1057) recipients achieved ≥ 4-fold rises against each of the 4 MenB strains (75.8–94.7% vs 67.4–95.0%) and titers reaching at least the lower limit of quantification against all 4 strains combined (79.9% vs 74.3%; **Figure 1A**). MenABCWY was noninferior to MenB-FHbp for all 5 endpoints. MenABCWY was also noninferior to a single MenACWY-CRM dose with 75.5–96.9% and 93.0–97.4% of MenABCWY recipients after dose 1 or 2, respectively, achieving ≥ 4-fold rises against serogroup A, C, W and Y depending on prior MenACWY experience (**Figure 1B**). Local reactions and systemic events after MenABCWY or MenB-FHbp were similarly frequent, mostly mild/moderate in severity (**Figure 2**), and unaffected by MenACWY experience.

Figure 1. Immune Responses as Measured in hSBA to (A) MenB Test Strains at 1 Month After Dose 2 and (B) MenA, MenC, MenW, and MenY Test Strains at 1 Month After Doses 1 and 2



Error bars represent 95% CIs. MenB strains note FHbp variants in parentheses.
*MenABCWY, n=418–432; MenB-FHbp, n=814–850.
†Composite response=hSBA titer ≥LLOQ for all 4 MenB test strains.
‡MenABCWY, n=227–262; MenACWY-CRM, n=446–506.
§MenABCWY, n=187–257; MenACWY-CRM, n=370–495.
hSBA=serum bactericidal activity with human complement; MenA=meningococcal serogroup A; LLOQ=lower limit of quantitation; m=month; MenABCWY=pentavalent serogroups A, B, C, W, Y vaccine; MenACWY-CRM=Menveo®, quadrivalent meningococcal CRM vaccine; MenB=meningococcal serogroup B; MenB-FHbp=Trumenba®, bivalent rLP2086; MenC=meningococcal serogroup C; MenW=meningococcal serogroup W; MenY=meningococcal serogroup Y; PD=postdose.

Figure 2. (A) Local Reactions and (B) Systemic Events Reported Within 7 Days After Any Dose



MenABCWY, n=542; MenB-FHbp+MenACWY-CRM, n=1050.
*At the MenABCWY/MenB-FHbp injection site.
MenABCWY=pentavalent serogroups A, B, C, W, Y vaccine; MenACWY-CRM=Menveo®, quadrivalent meningococcal CRM vaccine; MenB-FHbp=Trumenba®, bivalent rLP2086.

Conclusion: MenABCWY 4-fold immune responses from baseline were robust and noninferior to MenB-FHbp and MenACWY-CRM administered separately. Vaccination was safe and well tolerated. The favorable benefit-risk profile supports further MenABCWY development as a simplified alternative to current meningococcal vaccination practices. Funded by Pfizer.

Disclosures: **James Peterson, MD**, **Pfizer** (Scientific Research Study Investigator) **Daniel Drazan, MD**, **Pfizer** (Scientific Research Study Investigator) **Hanna Czajka, MD, PhD**, **Pfizer** (Scientific Research Study Investigator) **Jason Maguire, MD**, **Pfizer** (Employee, Shareholder) **Jean-Louis Pregaldien, MS**, **Pfizer** (Employee, Shareholder) **Ilkka Seppa, MD**, **Pfizer** (Scientific Research Study Investigator) **Roger Maansson, MS**, **Pfizer** (Employee, Shareholder) **Robert O'Neill, PhD**, **Pfizer** (Employee, Shareholder) **Annaliesa S. Anderson, PhD**, **Pfizer** (Employee, Shareholder) **Paul Balmer, PhD**, **Pfizer Inc** (Employee, Shareholder) **Johannes Beeslaar, MD**, **Pfizer** (Employee, Shareholder) **John L. Perez, MD, MA**, **Pfizer Inc** (Employee, Shareholder)