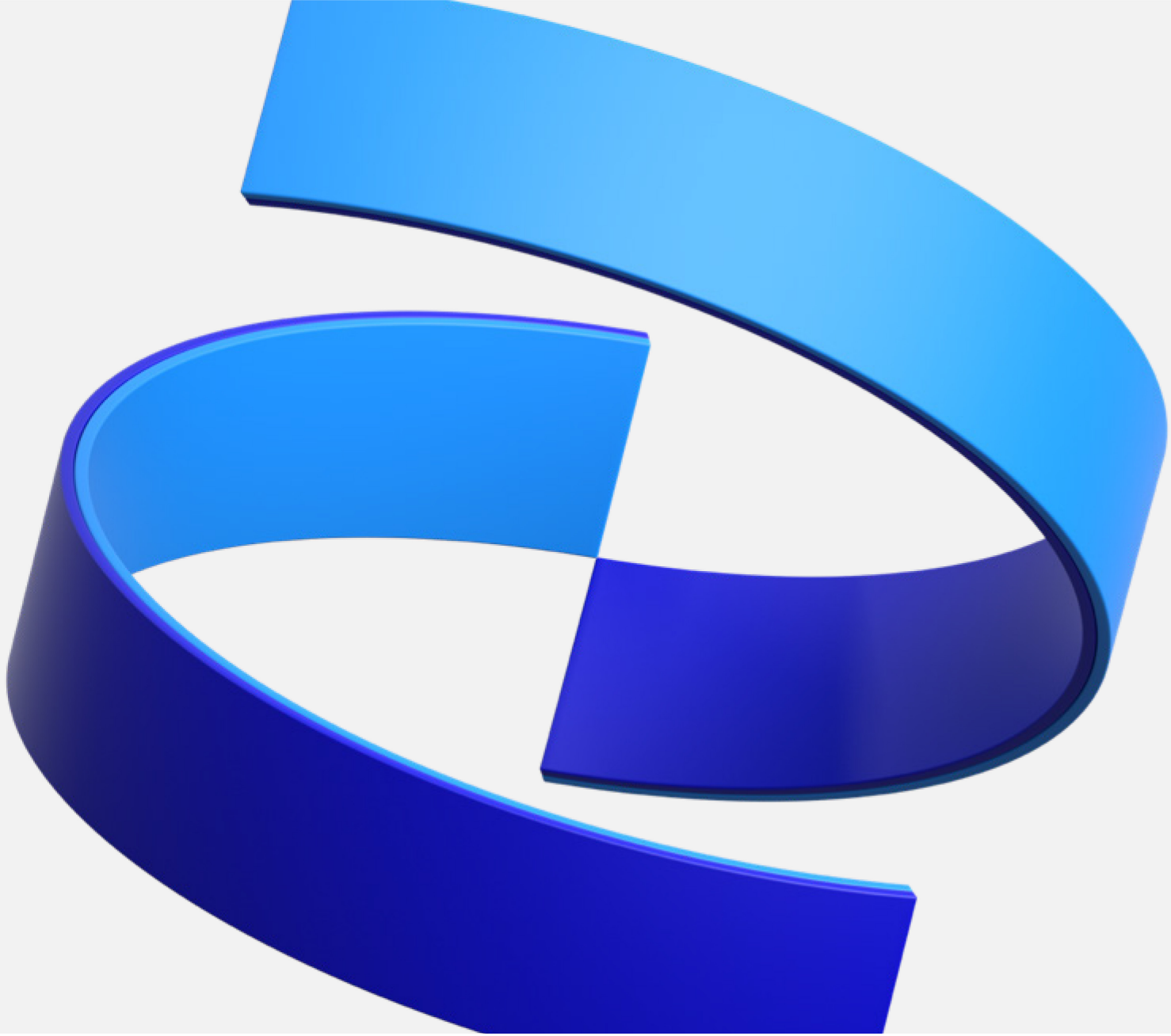
MenABCWY Meningococcal Vaccine



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Pfizer Vaccines Clinical R&D

MenABCWY Vaccine Overview

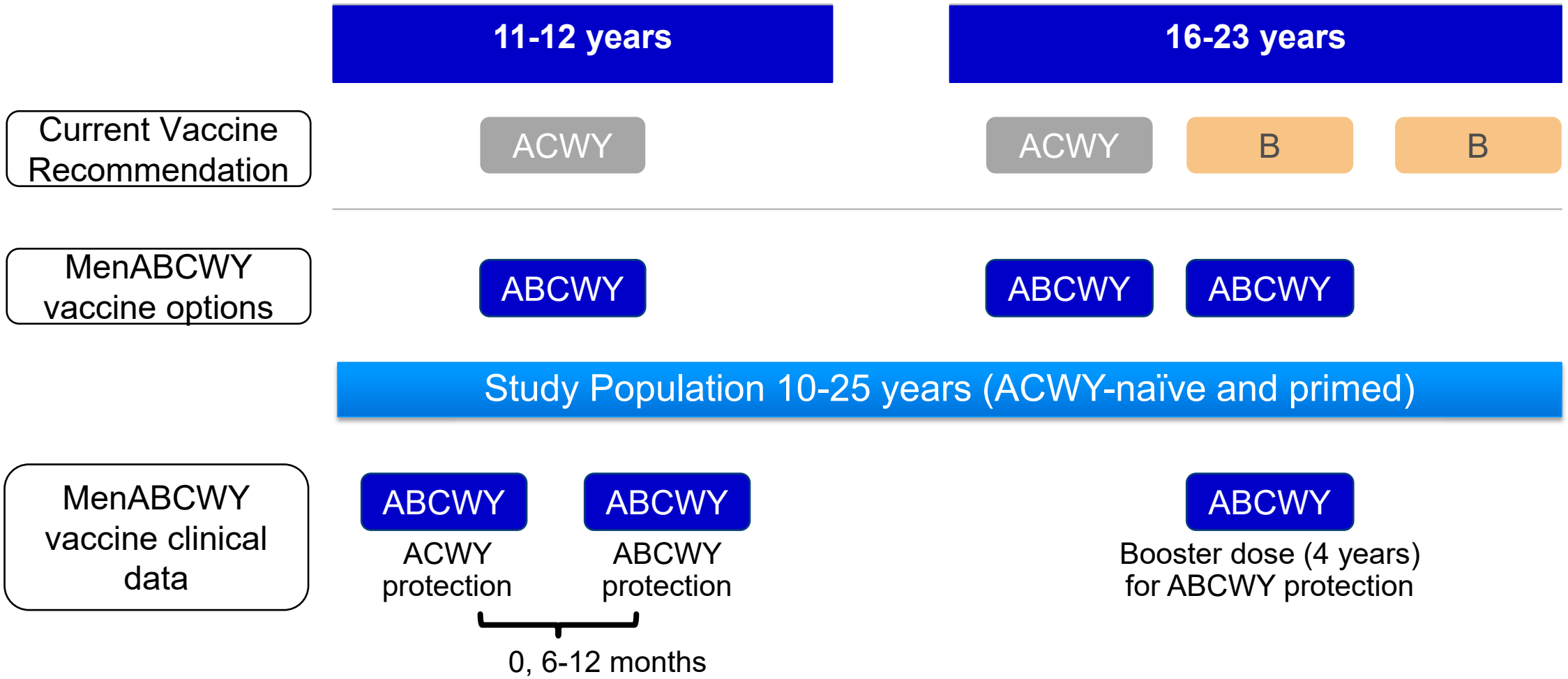
Indication and dosing being sought for MenABCWY vaccine

- Active immunization of individuals 10 through 25 years of age against invasive meningococcal diseases caused by *Neisseria meningitidis* serogroups A, B, C, W, Y
- Dosing:
  - Administer two doses at least 6 months apart for prevention of meningococcal disease caused by serogroups A, B, C, W and Y.
  - Administer one dose for prevention of meningococcal disease caused by serogroups A, C, W and Y.
  - A booster dose may be administered to individuals who have previously completed a primary series with MenABCWY or MenB-fHbp vaccine or who have previously received MenACWY conjugated vaccines

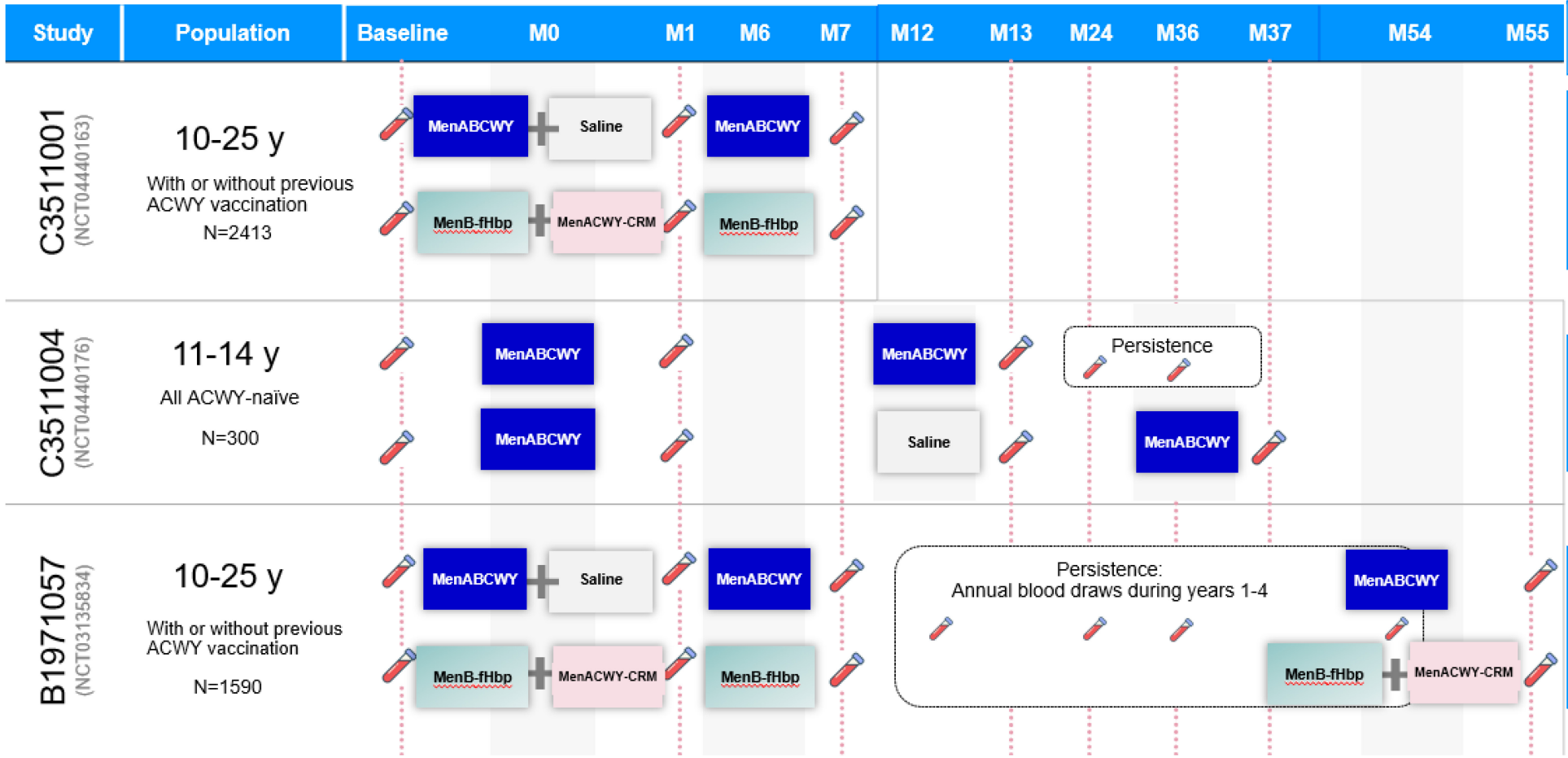
MenABCWY vaccine composition

- MenABCWY vaccine is composed of drug substance from:
  - Trumenba® (MenB-fHbp): licensed in the US for the prevention of invasive disease caused by *Neisseria meningitidis* group B in individuals 10 through 25 years of age
  - Nimenrix® (MenACWY-TT): licensed ex-US for the prevention of invasive disease caused by *Neisseria meningitidis* serogroups A, C, W, and Y in individuals 6 weeks of age and older.

Adolescent meningococcal vaccination platform options for MenABCWY vaccine



MenABCWY vaccine clinical program overview



Key immunogenicity (hSBA) data to be discussed

- **ABCWY responses after 2 doses (0,6m)**
- **ACWY responses after 1 dose**

- **ABCWY responses after 2 doses (0,12m)**

- **ABCWY 4-year persistence and booster response**

- All participants were meningococcal serogroup B vaccine naïve prior to study entry
- 80% of participants in the Phase 3 study were Caucasian; 10% black and African Americans; 25% of participants being Hispanic or Latino

Blood vial image source: Flaticon.com

Immunogenicity

Immunogenicity objectives and endpoints

FDA agreement for licensure

ACWY evaluation (non-inferiority after 1 and 2 doses of MenABCWY vaccine versus MenACWY-CRM)

- hSBA seroresponse* (4-fold)
- Naïve and primed participants

B evaluation (non-inferiority after 2 doses of MenABCWY vaccine versus MenB-fHbp)

- hSBA seroresponse* (4-fold)
- Composite response†

ABCWY evaluation (Other endpoints)

- hSBA thresholds (1:4, 1:8, 1:16)
- GMTs

MenB immunogenicity analysis: Same approach taken as for Trumenba licensure in the US

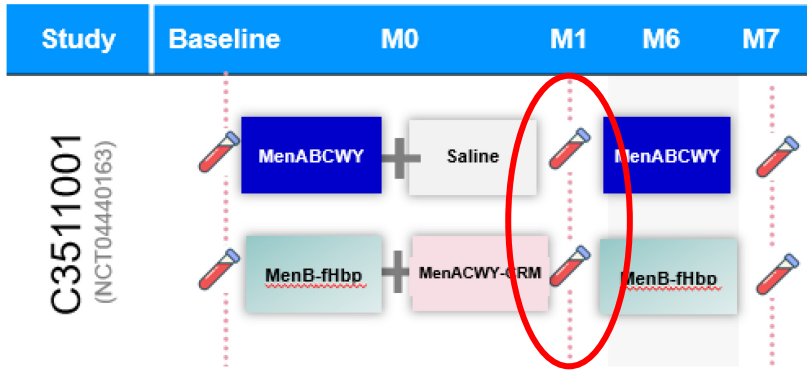
- **4 MenB test strains utilized,** 2 from Factor H Binding Protein (fHbp) subfamily A (A22, A56) and 2 from subfamily B (B24, B44)
- **hSBA results provide information on breadth of coverage against MenB strains**
- All strains express **vaccine-heterologous fHbp variants**
- **Strains and fHbp variants** expressed are representative of known genetic diversity; strains were randomly selected
- hSBA seropositivity defined as titers ≥1:8 or ≥1:16, which is greater than the 1:4 correlate of protection

Abbreviations: hSBA=human serum bactericidal assay; GMT=geometric mean titer; MenB=serogroup B

*For participants with a baseline hSBA titer <1:4, seroresponse is defined as a titer ≥1:16. For those with a baseline hSBA titer ≥1:4 and <1:8 (<1:16 for A22), seroresponse is a titer ≥4 times the 1:8 (1:16 for A22). For those with a baseline hSBA titer ≥1:8 (≥1:16 for A22), seroresponse is a titer ≥4 times the baseline titer. †hSBA titer ≥1:8 (1:16 for A22) for all 4 primary strains 1 month after Dose 2.

Immunogenicity ACWY-naive

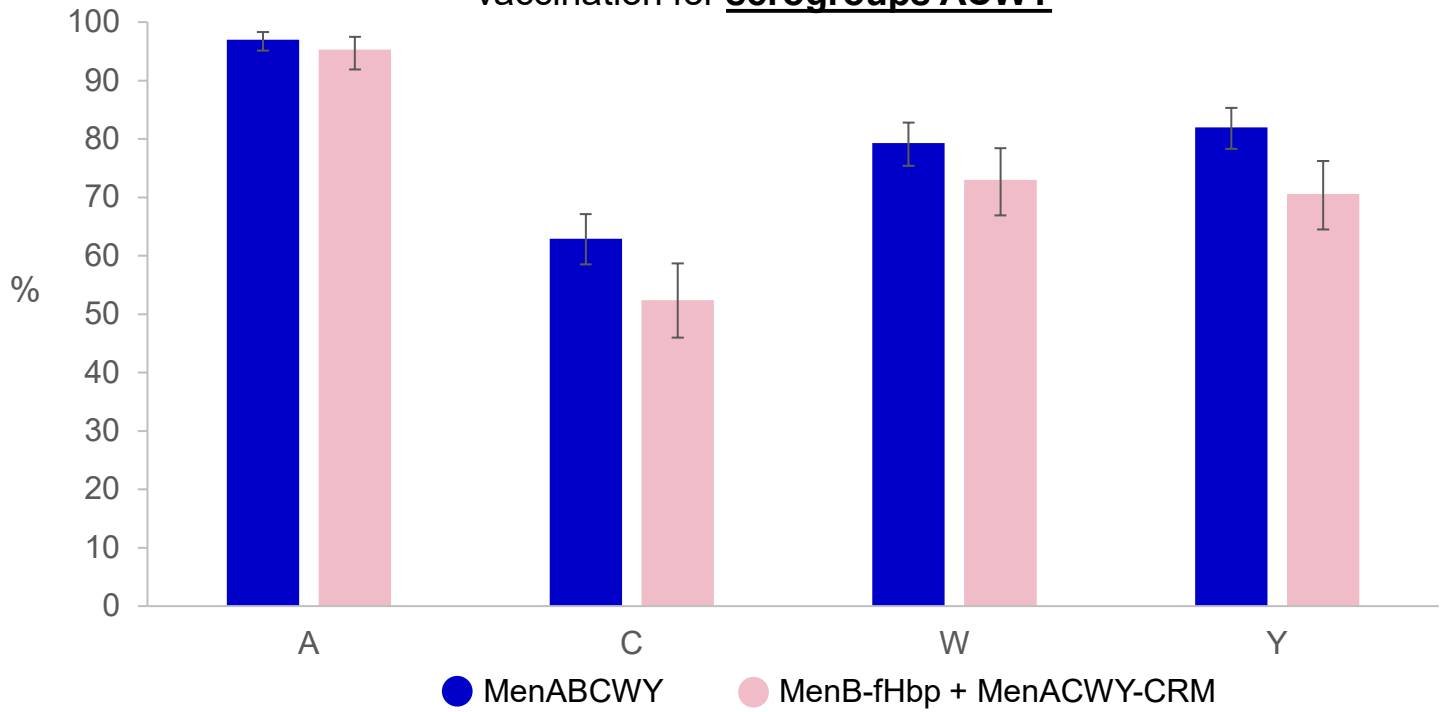
A single dose of MenABCWY vaccine can be used as an alternative to ACWY vaccines in ACWY-naïve adolescents



Comparisons (ACWY-naïve participants):

- MenABCWY vaccine 1 month after first dose
- MenACWY-CRM 1 month after single dose

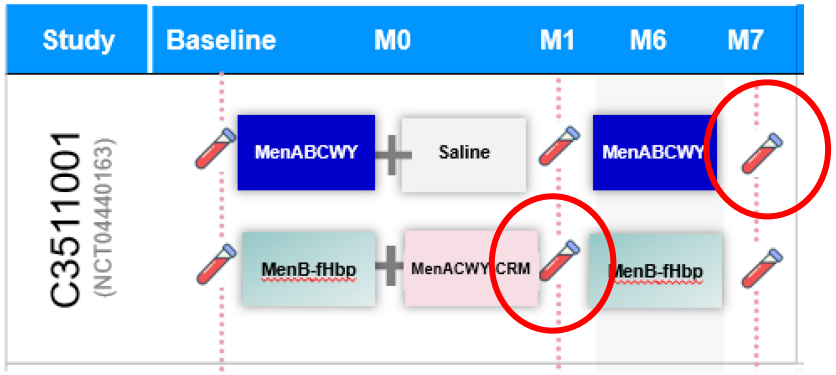
Percentage of participants achieving hSBA seroresponse* 1 month after vaccination for **serogroups ACWY**



- 1 dose of MenABCWY vaccine was noninferior to 1 dose of MenACWY-CRM in ACWY-naïve participants
- 82.4%-99.4% of participants had serogroups ACWY hSBA titers ≥1:8 after 1 dose of MenABCWY vaccine

Abbreviations: hSBA=serum bactericidal assay using human complement.
*For participants with a baseline hSBA titer <1:4, seroresponse is defined as a titer ≥1:16. For those with a baseline hSBA titer ≥1:4 and <1:8, seroresponse is a titer ≥4 times the 1:8. For those with a baseline hSBA titer ≥1:8, seroresponse is a titer ≥4 times the baseline titer.
N=492-501 for MenABCWY group; N=244-254 for MenB-fHbp + MenACWY-CRM group.
Data on File, Study C3511001 (NCT04440163) Aug 2022, Pfizer Inc.

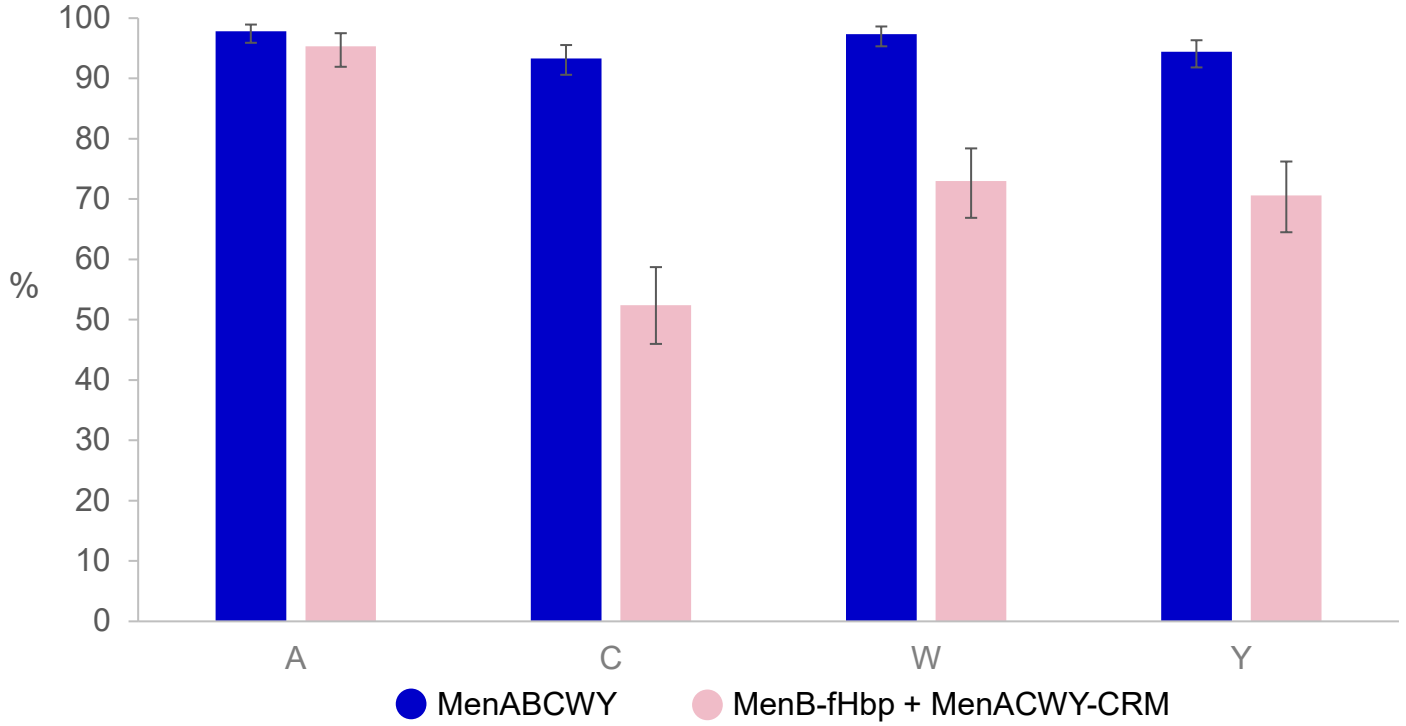
2 doses of MenABCWY vaccine elicit higher responses versus a single dose of MenACWY-CRM in ACWY-naïve participants



Comparisons (ACWY-naïve participants):

- MenABCWY vaccine 1 month after second dose
- MenACWY-CRM 1 month after single dose

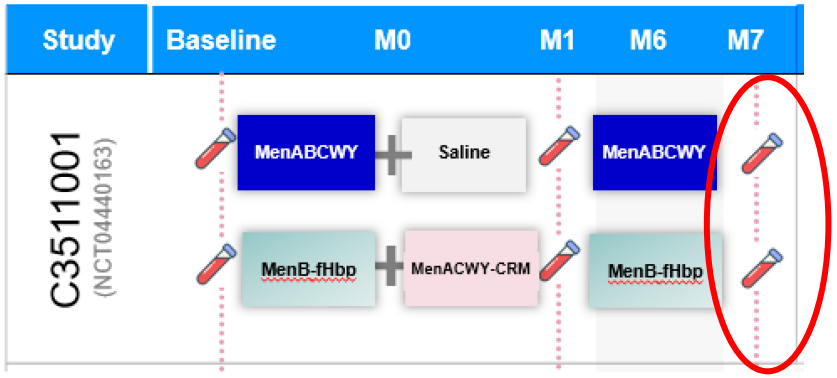
Percentage of participants achieving hSBA seroresponse* 1 month after vaccination for **serogroups ACWY**



- 2 doses of MenABCWY vaccine were noninferior to 1 dose of MenACWY-CRM in ACWY-naïve participants
- 99.1-99.8% of participants had serogroups ACWY hSBA titers ≥1:8 after 2 doses of MenABCWY vaccine

Abbreviations: hSBA=serum bactericidal assay using human complement.
*For participants with a baseline hSBA titer <1:4, seroresponse is defined as a titer ≥1:16. For those with a baseline hSBA titer ≥1:4 and <1:8, seroresponse is a titer ≥4 times the 1:8. For those with a baseline hSBA titer ≥1:8, seroresponse is a titer ≥4 times the baseline titer.
N=439-451 or MenABCWY group; N=244-254 for MenB-fHbp + MenACWY-CRM group.
Data on File, Study C3511001 (NCT04440163) Aug 2022, Pfizer Inc.

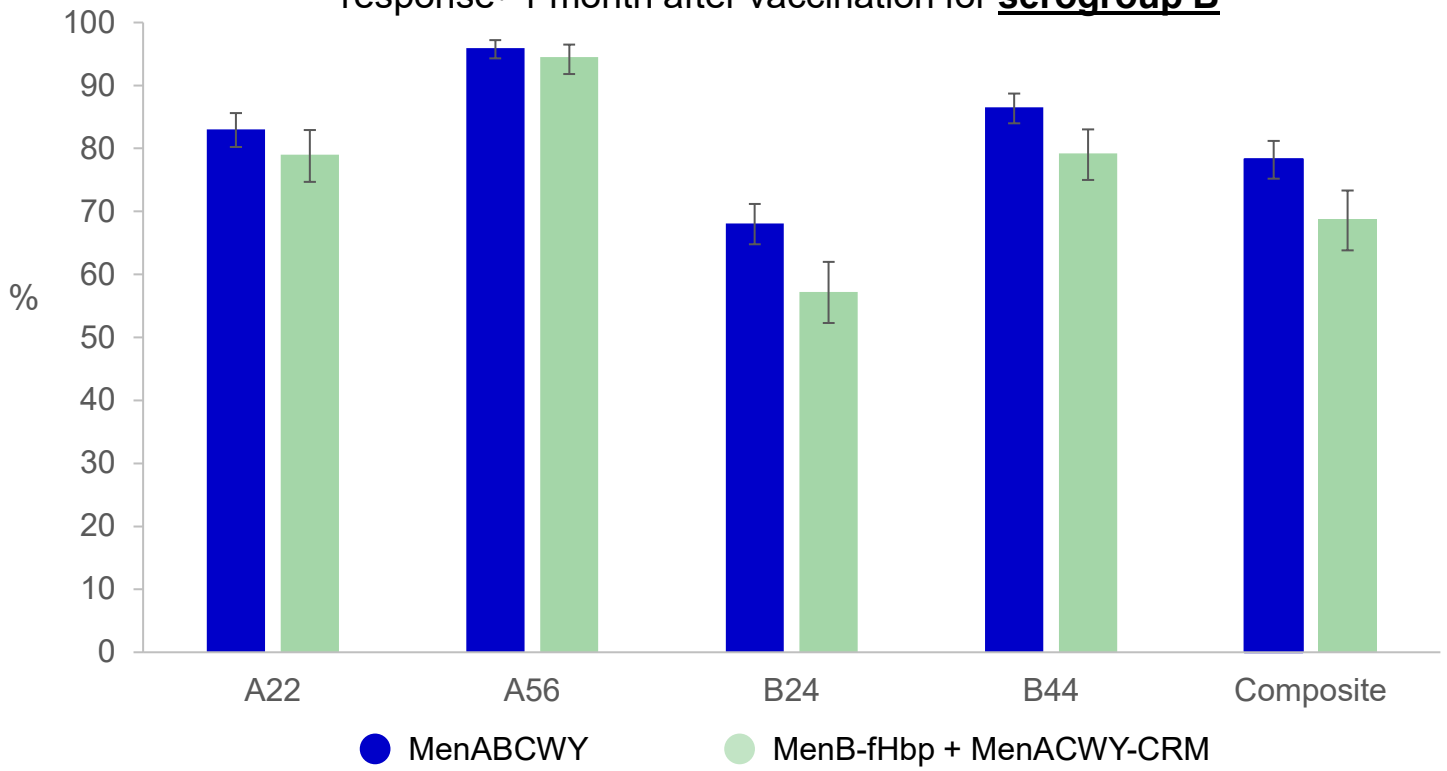
2 doses of MenABCWY vaccine elicit higher responses versus 2 doses of MenB-fHbp in B-naïve participants



Comparisons (B-naïve participants):

- MenABCWY vaccine 1 month after second dose
- MenB-fHbp 1 month after second dose

Percentage of participants achieving hSBA seroresponse* and composite response† 1 month after vaccination for **serogroup B**



- 2 doses of MenABCWY vaccine were noninferior to 2 doses of MenB-fHbp
- 83.4-98.7% of participants had serogroup B hSBA titers ≥1:8^ after 2 doses of MenABCWY vaccine

Abbreviations: hSBA=serum bactericidal assay using human complement.
*For participants with a baseline hSBA titer <1:4, seroresponse is defined as a titer ≥1:16. For those with a baseline hSBA titer ≥1:4 and <1:8 (<1:16 for A22), seroresponse is a titer ≥4 times the 1:8 (1:16 for A22). For those with a baseline hSBA titer ≥1:8 (≥1:16 for A22), seroresponse is a titer ≥4 times the baseline titer. †hSBA titer ≥1:8 (≥1:16 for A22) for all 4 MenB strains 1 month after Dose 2. ^≥1:16 for A22 strain
N=755-845 for MenABCWY group; N=383-419 for MenB-fHbp + MenACWY-CRM group.
Data on File, Study C3511001 (NCT04440163) Aug 2022, Pfizer Inc.

MenABCWY vaccine protects against all 5 serogroups with 2 doses given 6 to 12 months apart

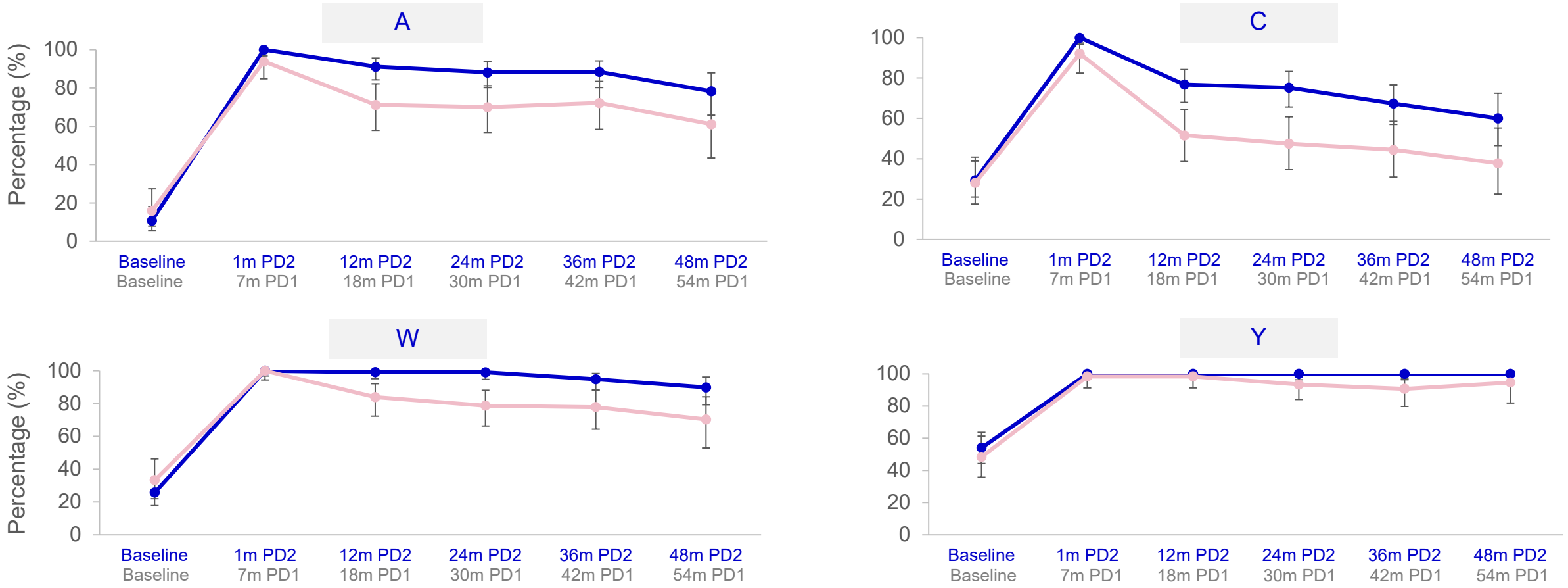
Seroresponse* 1m PD2	MenABCWY 0, 6m (Study 1001)			MenABCWY 0, 12m (Study 1004)		
Serogroups	**N^**	**%**	**95% CI**	**N^**	**%**	**95% CI**
A	447	**97.8**	95.9, 98.9	116	**99.1**	95.3, 100
C	451	**93.3**	90.6, 95.5	115	**99.1**	95.3, 100
W	439	**97.3**	95.3, 98.6	113	**99.1**	95.2, 100
Y	446	**94.4**	91.8, 96.3	111	**98.2**	93.6, 99.8
MenB strain						
A22	778	**83.0**	80.2, 85.6	111	**95.5**	89.8, 98.5
A56	807	**95.9**	94.3, 97.2	115	**100**	96.8, 100
B24	833	**68.1**	64.8, 71.2	113	**92.9**	86.5, 96.9
B44	845	**86.5**	84.0, 88.7	116	**94.8**	89.1, 98.1
MenB composite hSBA response†						
Before Dose 1	812	**1.2**	0.6, 2.3	114	**0.9**	0.0, 4.8
1 Month after Dose 2	755	**78.3**	75.2, 81.2	110	**96.4**	91.0, 99.0

- 2 doses of MenABCWY vaccine given 12 months apart elicit higher serogroup B responses
- 98.3-100% of participants had serogroups ABCWY hSBA titers ≥1:8 following 2 doses of MenABCWY vaccine given 12 months apart

Abbreviations: hSBA=serum bactericidal assay using human complement; MenB=serogroup B.
*For participants with a baseline hSBA titer <1:4, seroresponse is defined as a titer ≥1:16. For those with a baseline hSBA titer ≥1:4 and <1:8 (<1:16 for A22), seroresponse is a titer ≥4 times the 1:8 (1:16 for A22). For those with a baseline hSBA titer ≥1:8 (≥1:16 for A22), seroresponse is a titer ≥4 times the baseline titer. ^Number of subjects with valid and determinate hSBA titer for the given strain; for study 1001, population includes ACWY-naïve participants for serogroups ACWY. †hSBA titer ≥ 1:8 (1:16 for A22) for all 4 MenB strains 1 month after Dose 2.
Data on File, Study C3511001 (NCT04440163) and C3511004 (NCT04440176) Aug 2022, Pfizer Inc.

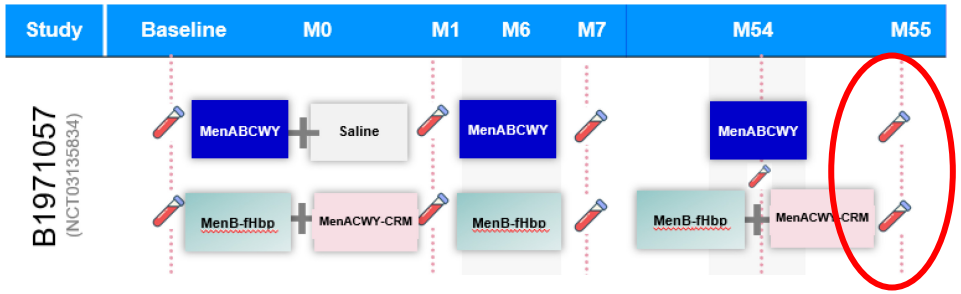
MenACWY seroprotection persists up to 4 years in ACWY-naïve participants

Percentage of individuals* with hSBA titers ≥ 1:8 at all timepoints



Abbreviations: hSBA=serum bactericidal assay using human complement; PB=post booster; PD1=post dose 1; PD2=post dose 2.
*Number of subjects with valid and determinate hSBA titer for the given strain ranged from 95-112 for MenABCWY and 54-64 for MenB-fHbp + MenACWY-CRM (Stage 2 mITT population [baseline through 36m PD2/42m PD1]), and 59-60 for MenABCWY and 36-37 for MenB-fHbp + MenACWY-CRM (Booster evaluable immunogenicity population [48m PD2 /54m PD1 Post Primary and Post Booster]).
Data on File, Study B1971057 (NCT03135834) Aug 2022, Pfizer Inc.

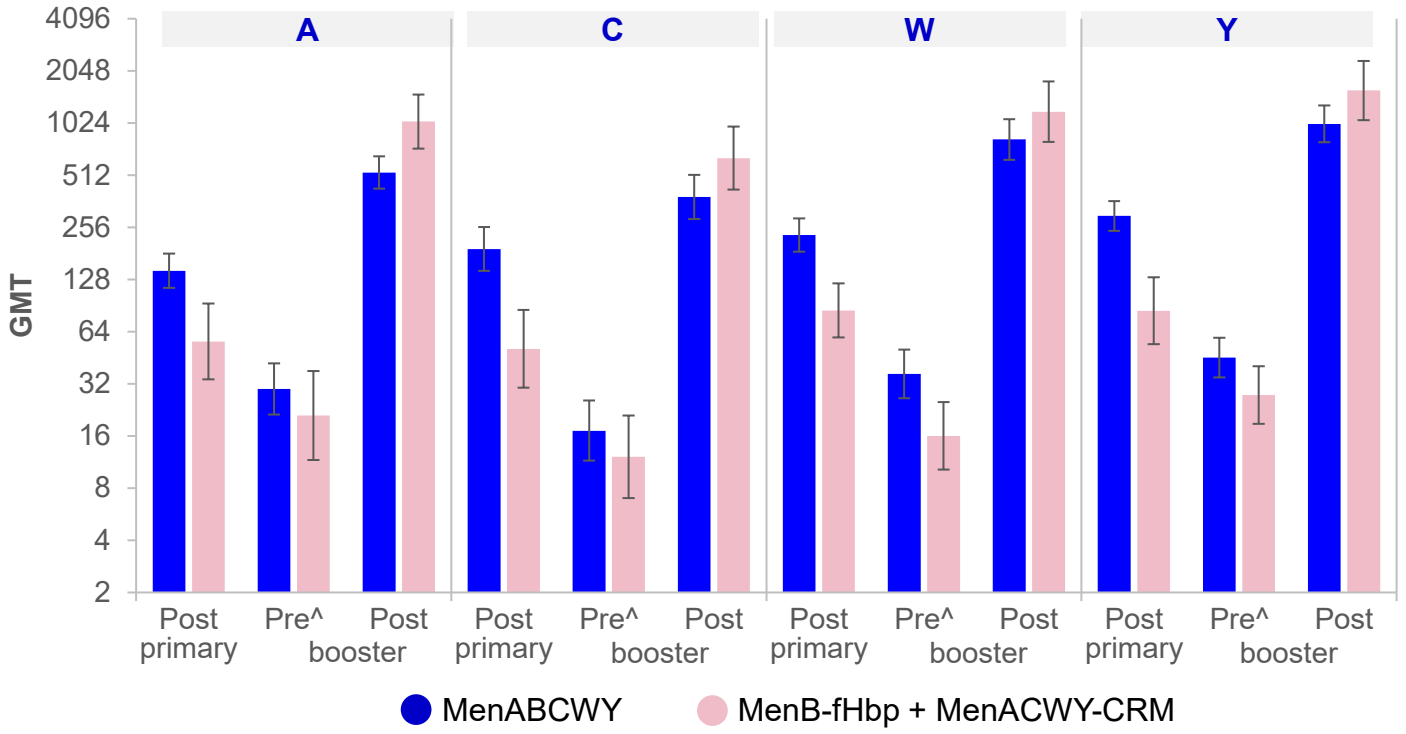
Booster response observed following a dose of MenABCWY vaccine 4 years after a 2 dose primary series (0,6m) in ACWY-naïve participants



Comparisons (ACWY-naïve participants):

- MenABCWY vaccine 4 years^ after second dose (pre booster) and 1 month after booster
- MenACWY-CRM 4.5 years^ after single dose (pre booster) and 1 month after booster

GMTs* 4 years after primary vaccination and 1 month after booster for **serogroups ACWY**

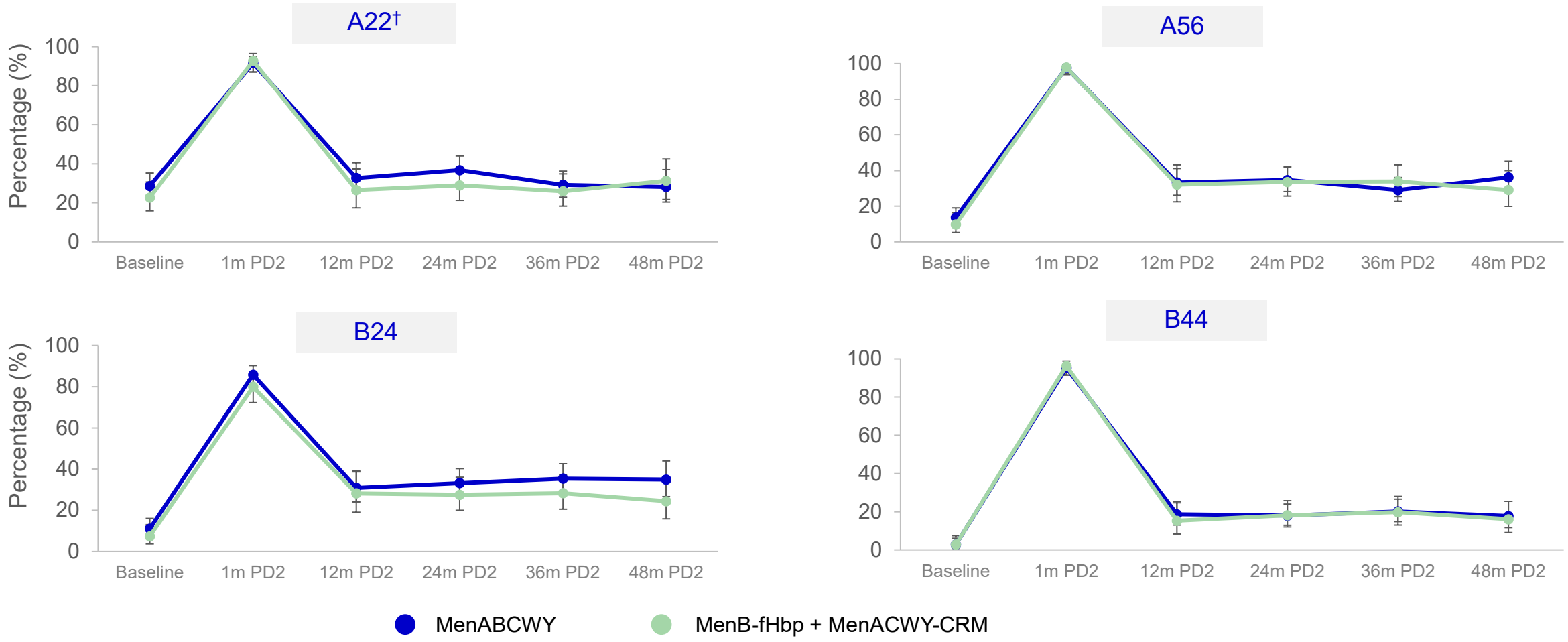


100% of participants had ACWY hSBA titers ≥1:8 following a booster dose of MenABCWY vaccine at 4 years

Abbreviations: hSBA=serum bactericidal assay using human complement; GMT= geometric mean titer; Post primary series =2 doses for MenABCWY and a single dose for MenACWY-CRM.
*Number of subjects with valid and determinate hSBA titer for the given strain ranged from 59-60 for MenABCWY and 35-37 for MenB-fHbp + MenACWY-CRM. ^Pre booster= 4 years after second dose of MenABCWY and 4.5 years after single dose of MenACWY-CRM.
Data on File, Study B1971057 (NCT03135834) Aug 2022, Pfizer Inc.

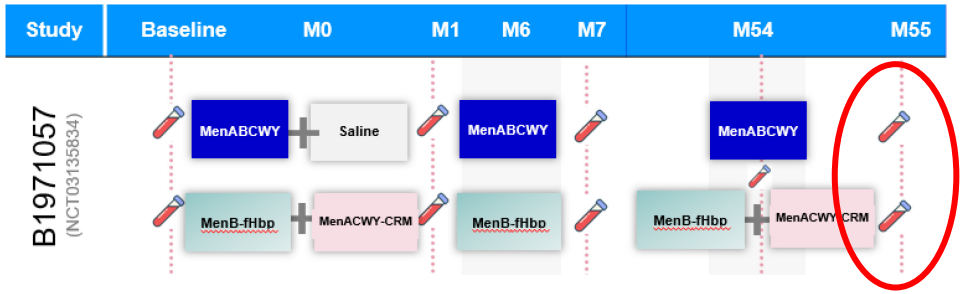
MenB seroprotection up to 4 years after 2 doses of MenABCWY

Percentage of individuals* with hSBA titers ≥ 1:8† at all timepoints



Abbreviations: hSBA=serum bactericidal assay using human complement; PD2=post dose 2.
*Number of subjects with valid and determinate hSBA titer for the given strain ranged from 162-212 for MenABCWY and 83-137 for MenB-fHbp + MenACWY-CRM (Stage 2 mITT population [baseline through 36m PD2]), and 121-129 for MenABCWY and 81-87 for MenB-fHbp + MenACWY-CRM (Booster evaluable immunogenicity population [48m PD2 Post Primary and Post Booster]).†hSBA ≥1:16 for A22.
Data on File, Study B1971057 (NCT03135834) Aug 2022, Pfizer Inc.

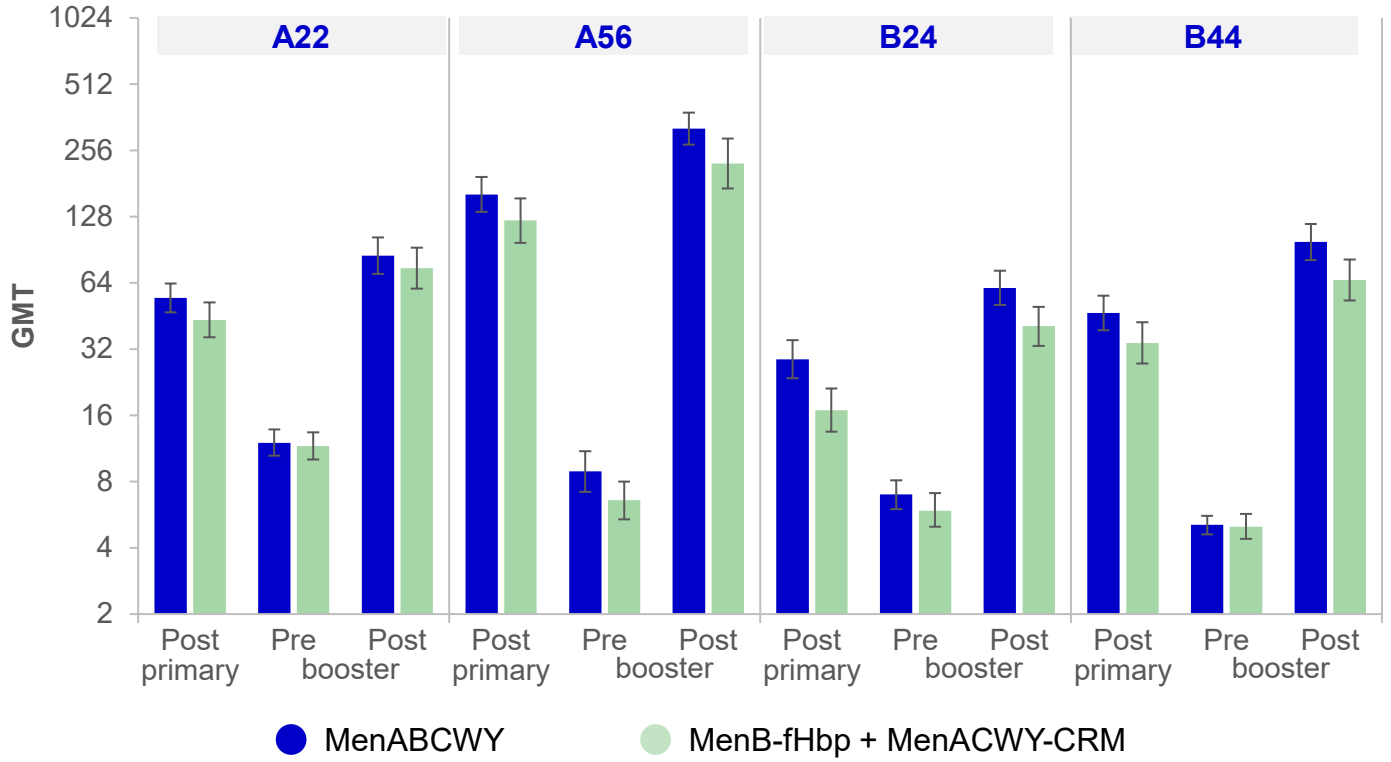
Booster response observed following a dose of MenABCWY vaccine 4 years after a 2 dose primary series (0,6m) in B-naïve participants



Comparisons (B-naïve participants):

- MenABCWY vaccine 4 years after second dose (pre booster) and 1 month after booster
- MenB-fHbp 4 years after second dose (pre booster) and 1 month after booster

GMTs* 4 years after primary vaccination and 1 month after booster for **serogroup B**

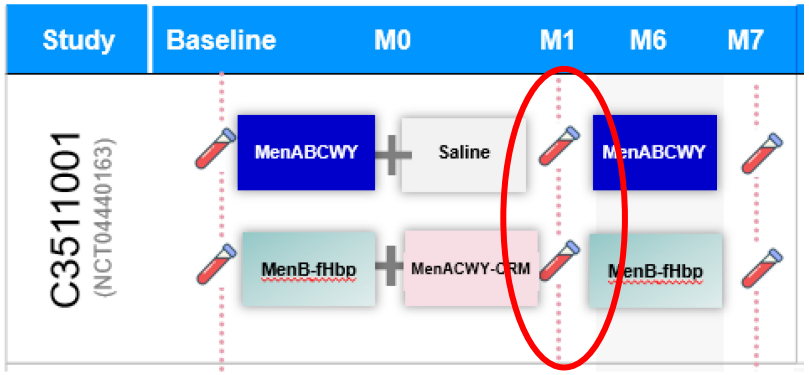


- 95.1-100% of participants had B hSBA titers ≥1:8^ following a booster dose of MenABCWY vaccine 4 years

Abbreviations: hSBA=serum bactericidal assay using human complement; GMT= geometric mean tier; Post primary series (2 doses for both MenABCWY and MenB-fHbp)
*Number of subjects with valid and determinate hSBA titer for the given strain ranged from 121-130 for MenABCWY and 81-88 for MenB-fHbp + MenACWY-CRM. ^≥1:16 for A22 strain
Data on File, Study B1971057 (NCT03135834) Aug 2022, Pfizer Inc.

Immunogenicity ACWY-primed

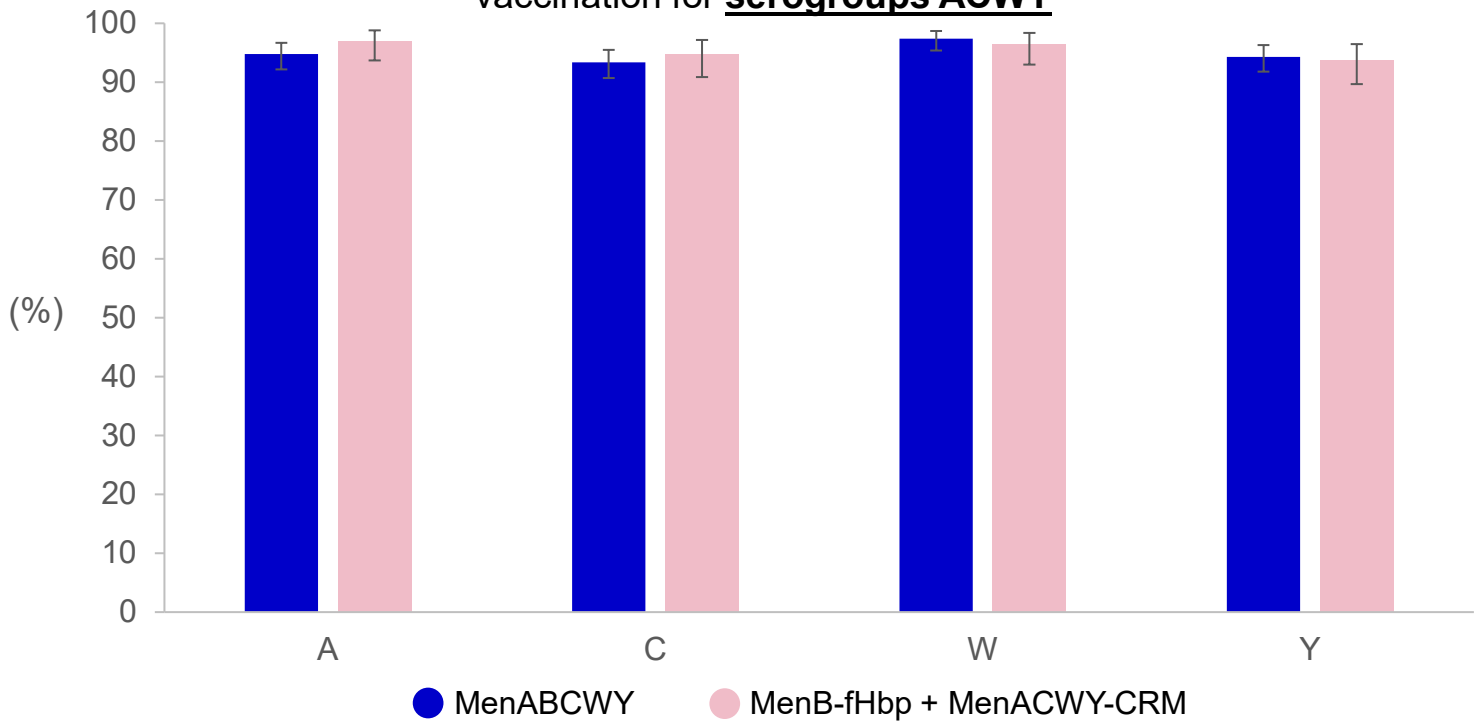
A single dose of MenABCWY vaccine can be used as an alternative to ACWY vaccines in ACWY-primed adolescents



Comparisons (ACWY-primed participants):

- MenABCWY vaccine 1 month after first dose
- MenACWY-CRM 1 month after single dose

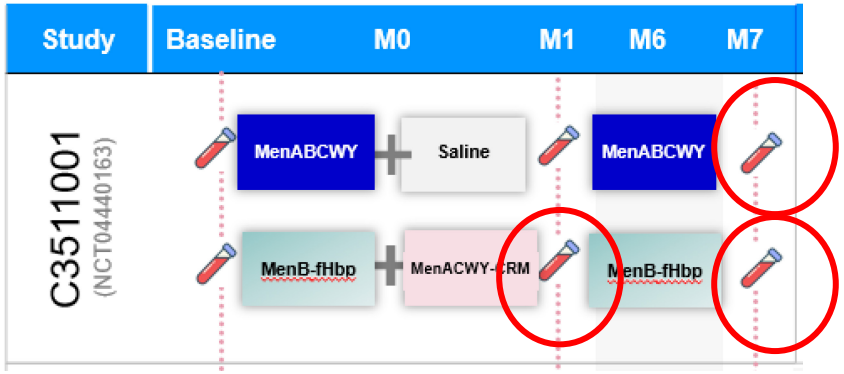
Percentage of participants achieving hSBA seroresponse* 1 month after vaccination for **serogroups ACWY**



- 1 dose of MenABCWY vaccine was noninferior to 1 dose of MenACWY-CRM in ACWY-primed participants
- 99.5-100% of participants had serogroups ACWY hSBA titers ≥1:8 after 1 dose of MenABCWY vaccine

Abbreviations: hSBA=serum bactericidal assay using human complement.
*For participants with a baseline hSBA titer <1:4, seroresponse is defined as a titer ≥1:16. For those with a baseline hSBA titer ≥1:4 and <1:8, seroresponse is a titer ≥4 times the 1:8. For those with a baseline hSBA titer ≥1:8, seroresponse is a titer ≥4 times the baseline titer.
N=428-442 for MenABCWY group; N=222-227 for MenB-fHbp + MenACWY-CRM group.
Data on File, Study C3511001 (NCT04440163) Aug 2022, Pfizer Inc.

2 doses of MenABCWY vaccine can be used as an alternative to 1 dose MenACWY-CRM and 2 doses MenB-fHbp in ACWY-primed adolescents



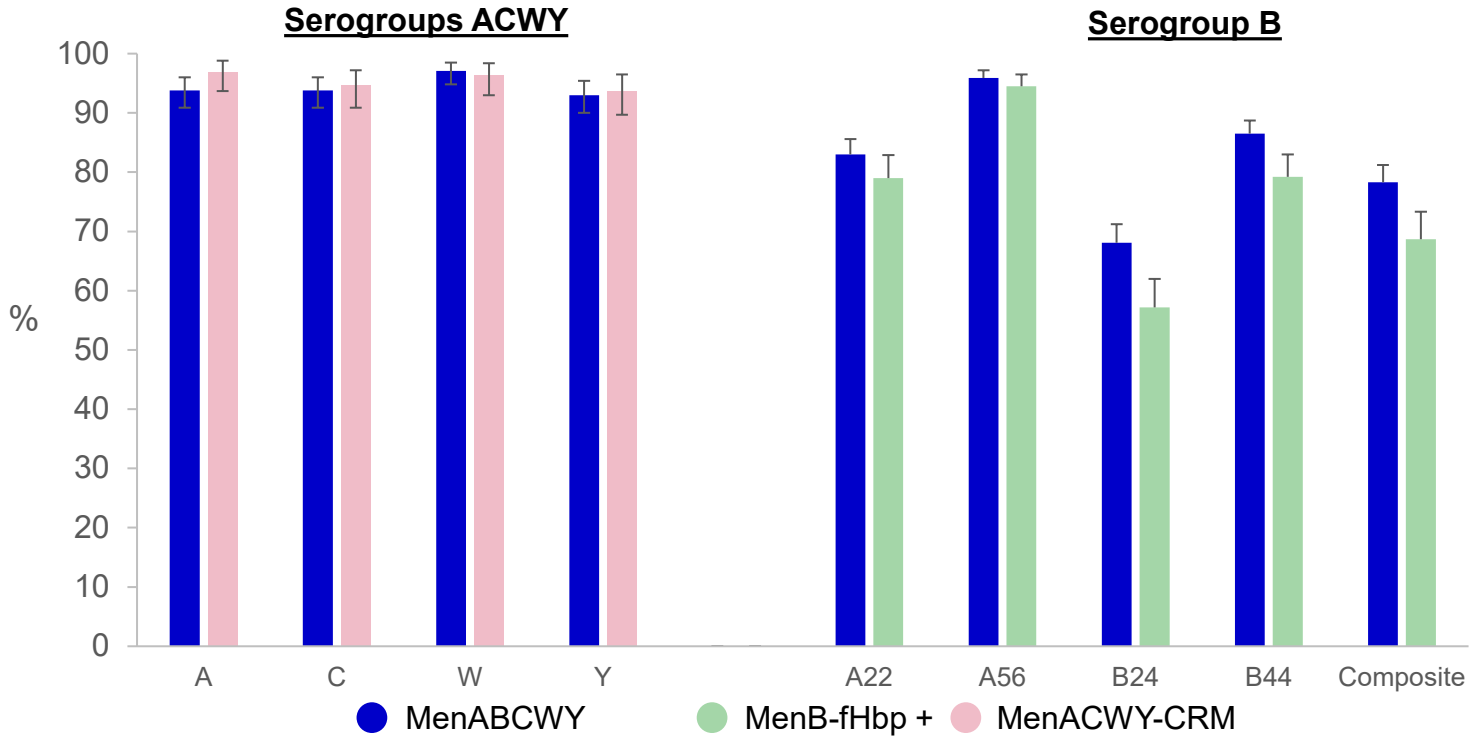
Comparisons (ACWY-primed participants):

- MenABCWY vaccine 1 month after second dose
- MenACWY-CRM 1 month after single dose

Comparisons (All participants group B vaccine naive):

- MenABCWY vaccine 1 month after second dose
- MenB-fHbp 1 month after second dose

Percentage of participants achieving hSBA seroresponse* 1 month after vaccination

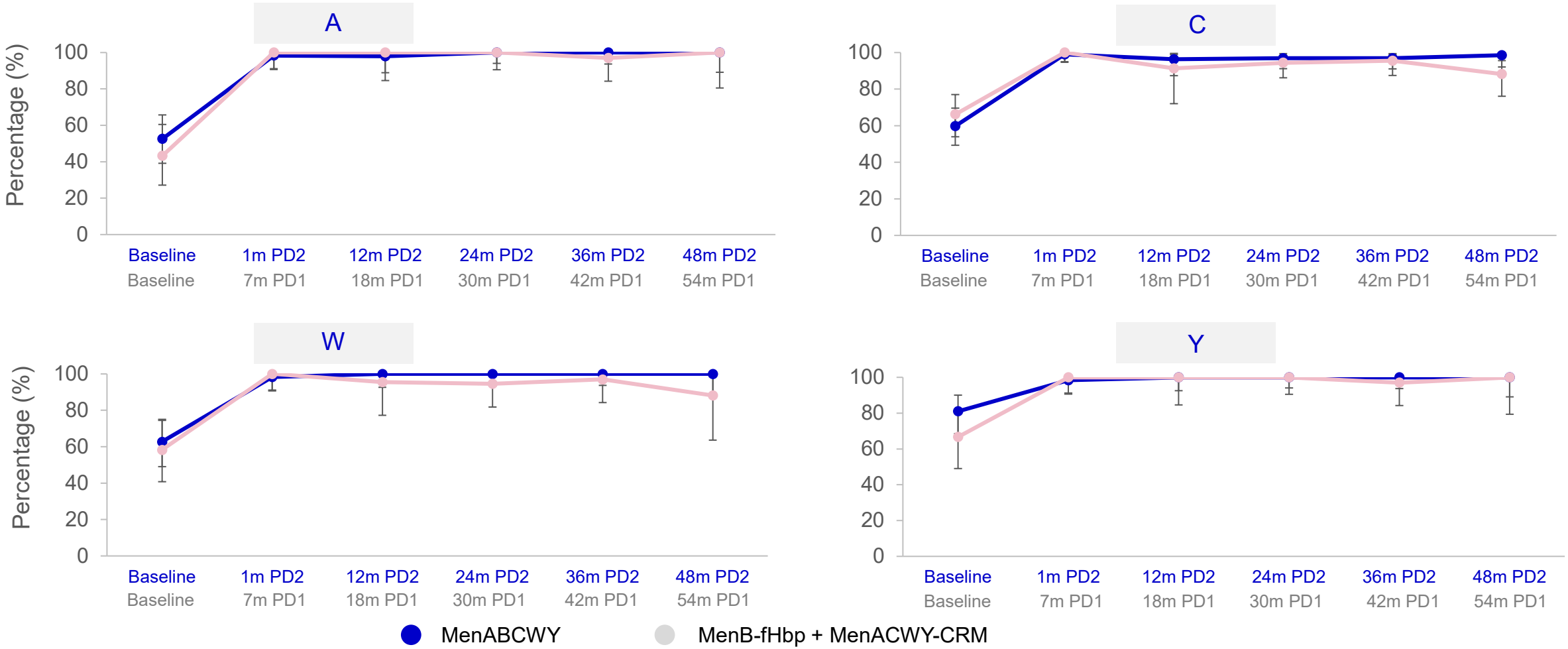


- 2 doses of MenABCWY vaccine were noninferior to 1 dose of MenACWY-CRM in ACWY-primed participants
  - 99-100% had serogroups ACWY hSBA titers ≥1:8 after 2 doses of MenABCWY vaccine
- 100% of ACWY-primed participants have protective titers four years after 2 doses of MenABCWY vaccine (Study B1971057)

Abbreviations: hSBA=serum bactericidal assay using human complement.
*For participants with a baseline hSBA titer <1:4, seroresponse is defined as a titer ≥1:16. For those with a baseline hSBA titer ≥1:4 and <1:8, seroresponse is a titer ≥4 times the 1:8. For those with a baseline hSBA titer ≥1:8, seroresponse is a titer ≥4 times the baseline titer.
N=376-387 for MenABCWY group; N=22-227 for MenB-fHbp + MenACWY-CRM group.
Data on File, Study C3511001 (NCT04440163) and Study B1971057 (NCT03135834) Aug 2022, Pfizer Inc

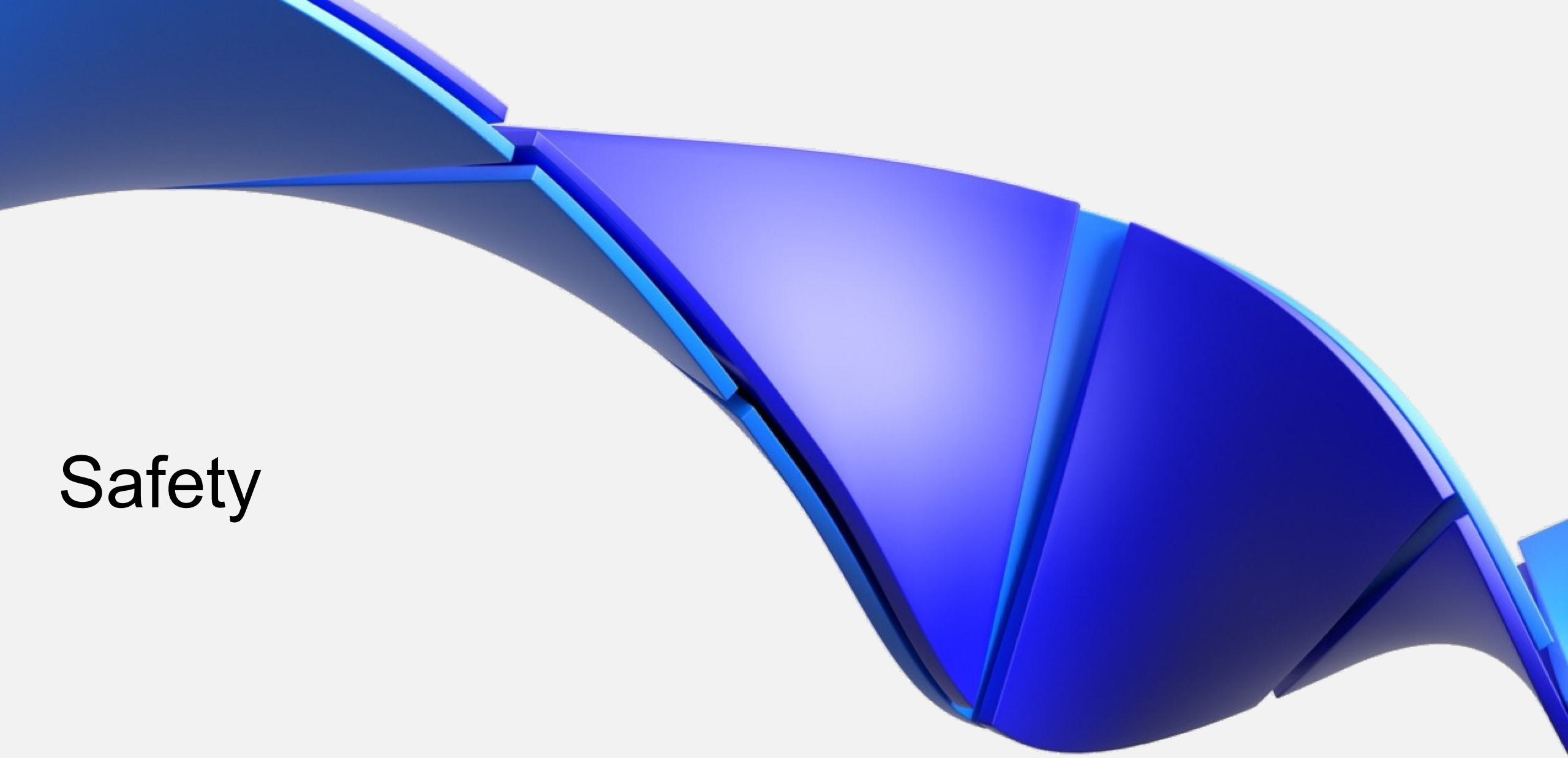
MenACWY seroprotection persists up to 4 years in ACWY-primed population

Percentage of participants* (95% CI) with hSBA titers ≥ 1:8

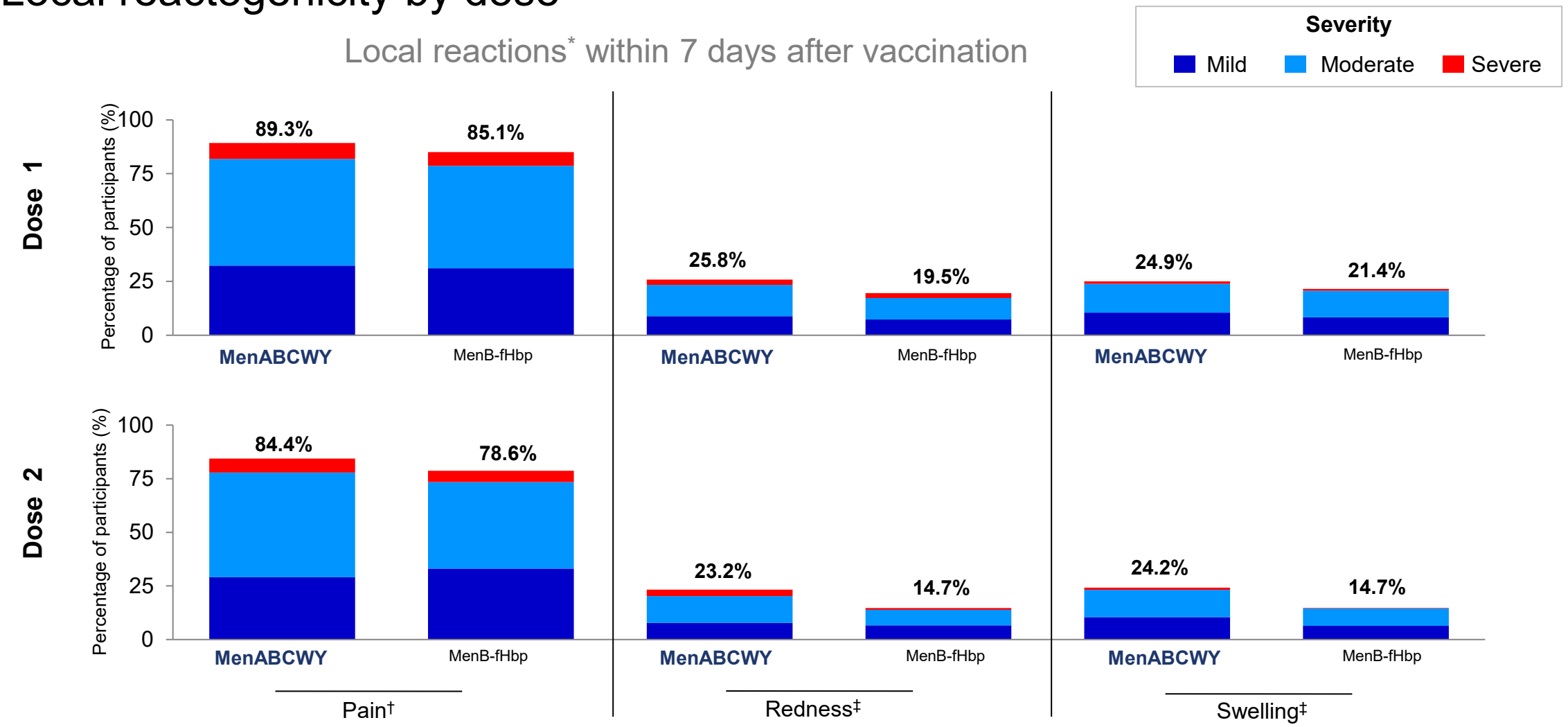


Abbreviations: hSBA=serum bactericidal assay using human complement; PB=post booster; PD1=post dose 1; PD2=post dose 2.
*Number of subjects with valid and determinate hSBA titer for the given strain. Lower N for groups A, W, Y compared to C due to receipt of monovalent C vaccine prior to study entry.
For groups A, W, and Y, N=48-61 for MenABCWY and 22-38 for MenB-fHbp + MenACWY-CRM (Stage 2 mITT population [baseline through 36m PD2/42m PD1]), and 32-33 for MenABCWY and 16-17 for MenB-fHbp + MenACWY-CRM (Booster evaluable immunogenicity population [48m PD2 /54m PD1 Post Primary and Post Booster]). For group C, N=54-100 for MenABCWY and 23-72 for MenB-fHbp + MenACWY-CRM (Stage 2 mITT population), and 68-70 for MenABCWY and 51 for MenB-fHbp + MenACWY-CRM (Booster evaluable immunogenicity population).
Data on File, Study B1971057 (NCT03135834) Aug 2022, Pfizer Inc.

Safety



Local reactogenicity by dose

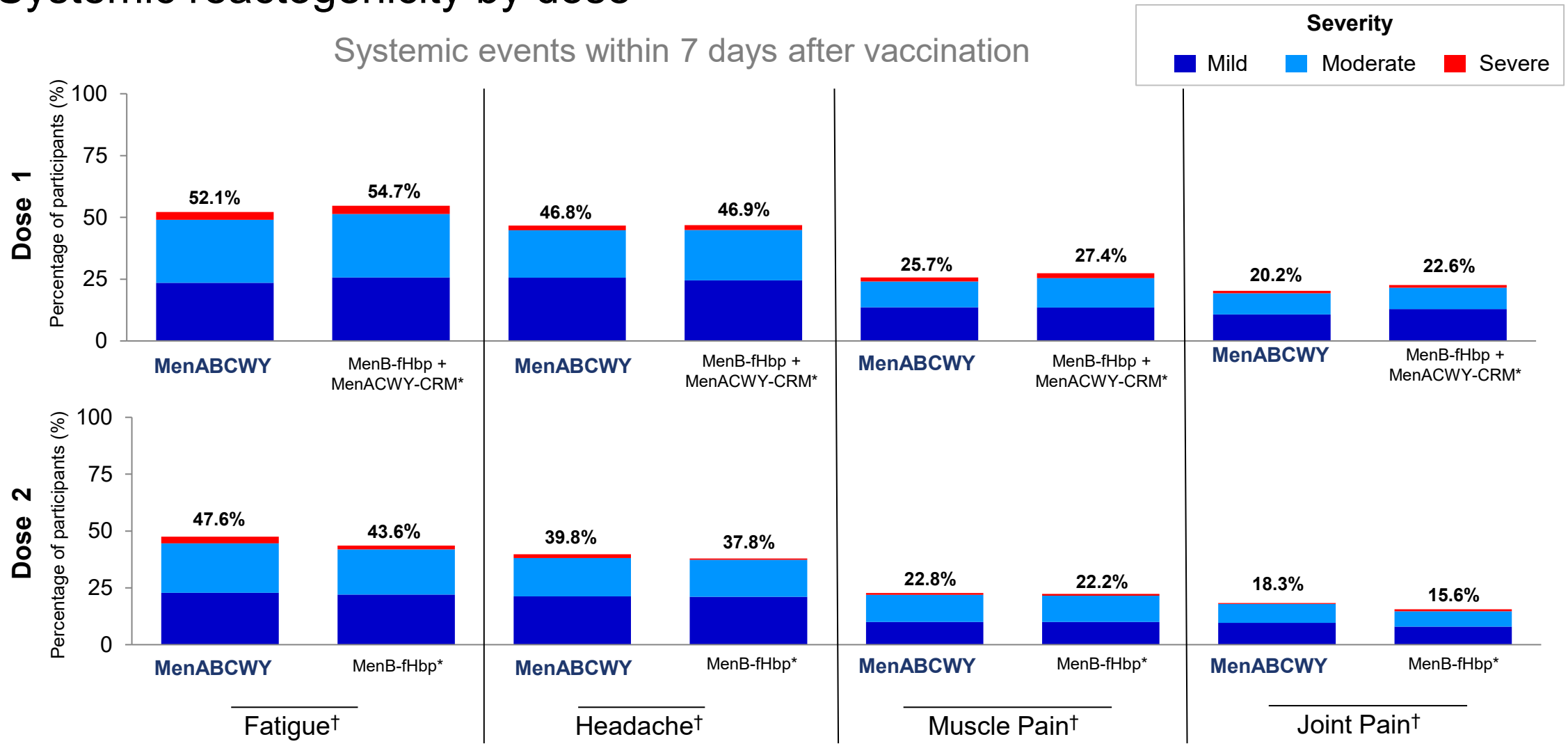


No differences observed between: ACWY-Naïve and Primed participants or Primary and Booster vaccination

*Local reactions are summarized only for the left arm, which is the MenABCWYvaccine or MenB+fHbp injection site; †Mild=does not interfere with activity, moderate=interferes with activity, severe=prevents daily activity.
‡Mild=>2.0 to 5.0 cm, moderate=>5.0 to 10.0 cm, and severe is >10.0 cm.
Data on File, Study C3511001 (NCT04440163) Aug 2022, Pfizer Inc.

10-25 years

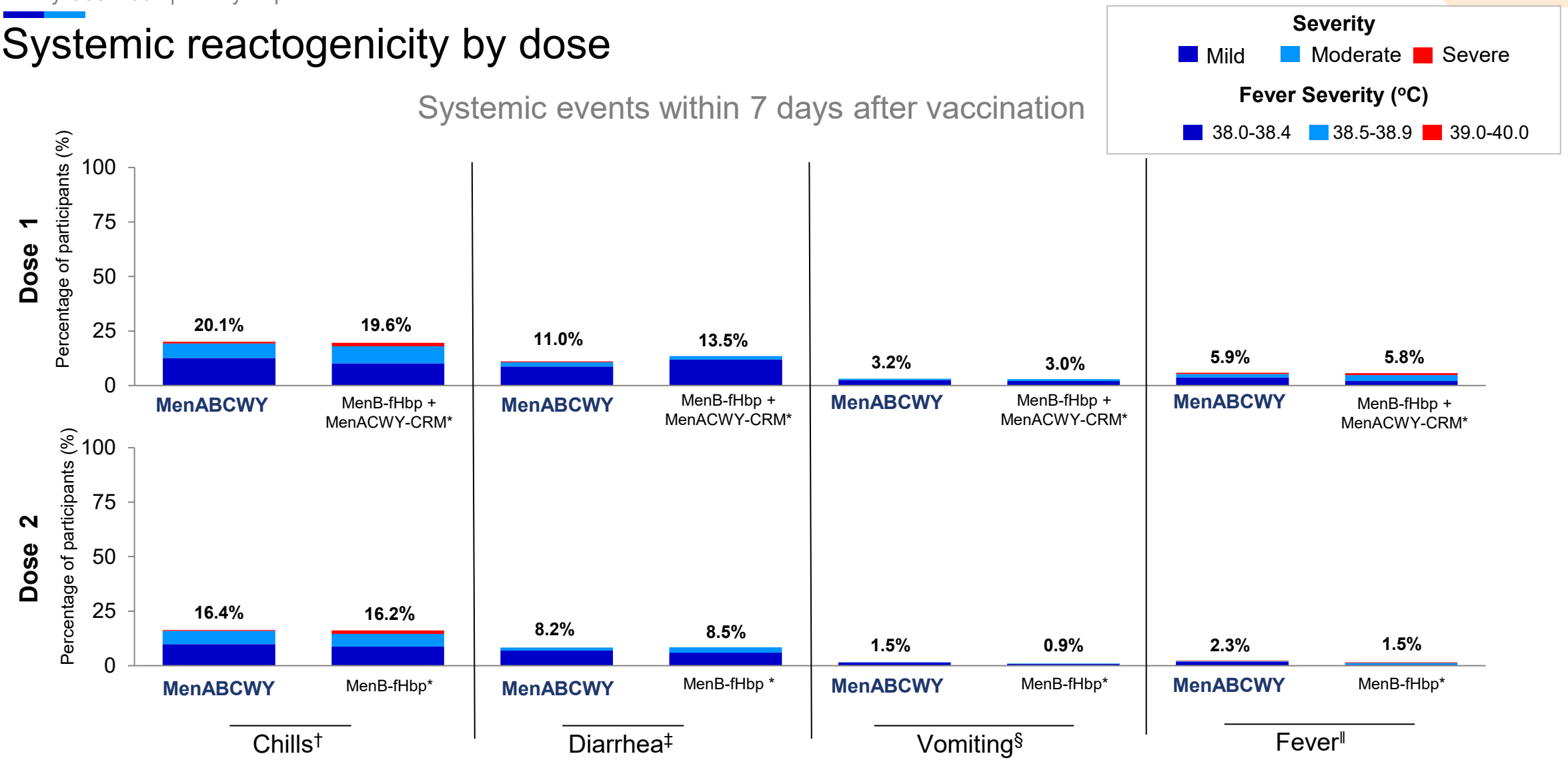
Systemic reactogenicity by dose



No differences observed between: ACWY-Naïve and Primed participants or Primary and Booster vaccination

*MenB-fHbp + MenACWY-CRM group: MenB-fHbp and MenACWY-CRM given at dose 1 and 3, MenB-fHbp given at dose 2.
†Mild: does not interfere with activity; Moderate: some interference with activity; Severe: prevents daily routine activity.
Data on File, Study C3511001 (NCT04440163) Aug 2022, Pfizer Inc.

Systemic reactogenicity by dose



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Number (%) of participants reporting ≥1 adverse event during the vaccination phase*

Endpoint	MenABCWY + Saline N=1763				MenB-fHbp + MenACWY-CRM N=649			
	n	%	(95% CI)	Number of Events	n	%	(95% CI)	Number of Events
All AEs	368	**20.9**	(19.0, 22.8)	638	132	**20.3**	(17.3, 23.6)	202
Related	11	**0.6**	(0.3, 1.1)	19	4	**0.6**	(0.2, 1.6)	5
Severe	13	**0.7**	(0.4, 1.3)	17	4	**0.6**	(0.2, 1.6)	4
All SAEs	7	**0.4**	(0.2, 0.8)	9	0	**0**	(0.0, 0.6)	0
Related	0	**0**	(0.0, 0.2)	0	0	**0**	(0.0, 0.6)	0
All MAEs	263	**14.9**	(13.3, 16.7)	436	93	**14.3**	(11.7, 17.3)	141
Related	2	**0.1**	(0.0, 0.4)	2	1	**0.2**	(0.0, 0.9)	1
Severe	8	**0.5**	(0.2, 0.9)	9	3	**0.5**	(0.1, 1.3)	3
All NDCMCs	20	**1.1**	(0.7, 1.7)	23	2	**0.3**	(0.0, 1.1)	2
Related	0	**0**	(0.0, 0.2)	0	0	**0**	(0.0, 0.6)	0
Severe	1	**<0.1**	(0.0, 0.3)	2	0	**0**	(0.0, 0.6)	0

Higher number of NDCMCs of ADHD in the MenABCWY group – most of them with ADHD-related symptoms before entering the study

Abbreviations: AE=adverse event; MAE=medically attended event (nonserious AE that results in an evaluation at a medical facility); NDCMC=newly diagnosed chronic medical condition (a disease or medical condition, not previously identified, that is expected to be persistent or is otherwise long-lasting in its effects); SAE=serious adverse event.
*Vaccination phase refers to the time from the first study vaccination (Visit 1) through 1 month after the second study vaccination (Visit 4).
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Overall conclusion: Data support the use of MenABCWY vaccine in the US adolescent meningococcal vaccination platform

Safety

- MenABCWY vaccine was safe and well tolerated in adolescents and young adults

ACWY protection

- A single dose of MenABCWY vaccine can be used as an alternative to ACWY vaccines in ACWY-naïve or primed adolescents and young adults

ABCWY protection

- MenABCWY vaccine protects against all 5 serogroups with 2 doses given 6 to 12 months apart
- Booster response was observed following a dose of MenABCWY vaccine 4 years after a 2 dose primary series (0,6m) for all 5 serogroups
- If 2 doses of MenABCWY vaccine are administered at 11-12 yrs of age, data support that a single (booster) dose from 16 years of age can provide protection against all 5 serogroups

Acknowledgements

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- The clinical trial participants
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