第47回厚生科学審議会予防接種・ワクチン分科会	参考資料2
2023(令和５)年６月16日	

FDA VRBPAC（６月15日開催）資料（一部抜粋）

※　事務局において、通し番号と関連する資料へ印を付与した。

Moderna COVID-19 Variant Vaccines

Moderna, Inc.

June 15, 2023

Vaccines and Related Biological Products Advisory Committee

Introduction

Rituparna Das, MD, PhD
Vice President, Clinical Development
Therapeutic Area Head, Respiratory Vaccines
Moderna, Inc.

Moderna Continues to Prepare and Evaluate New COVID-19 Vaccines as SARS-CoV-2 Variants Emerge

Moderna's Ongoing Commitment

- Monitor emerging Variants of Concern
- Develop new candidate vaccines
- Generate preclinical and clinical data accordingly
- Ensure manufacturing capabilities to rapidly respond to public health needs
- Prepared to supply new variant-containing vaccine as recommended

Recent Research Activities

- Authorized bivalent BA.4/5 vaccine
  - Assessed real-world effectiveness
  - Evaluated cross neutralization against emerging XBB variants
- Investigational XBB-containing vaccines
  - Developed at risk
  - Generated preclinical and clinical data

Effectiveness of Authorized Bivalent (Original + BA.4/5) COVID-19 Vaccine

Kaiser Permanente Southern California

Study 901

Methods

Study 901 - Kaiser Permanente Southern California Effectiveness Study

Study Design

- Matched cohort design
- 3 groups of adults ≥18 years (1:2:1 ratio)
  - Individuals who received ≥ 2 doses of any mRNA vaccine + Moderna BA.4/5 booster
  - Individuals who received ≥ 2 doses of any mRNA vaccine only
  - Unvaccinated individuals
- Matched on age, sex, race/ethnicity, and the index date

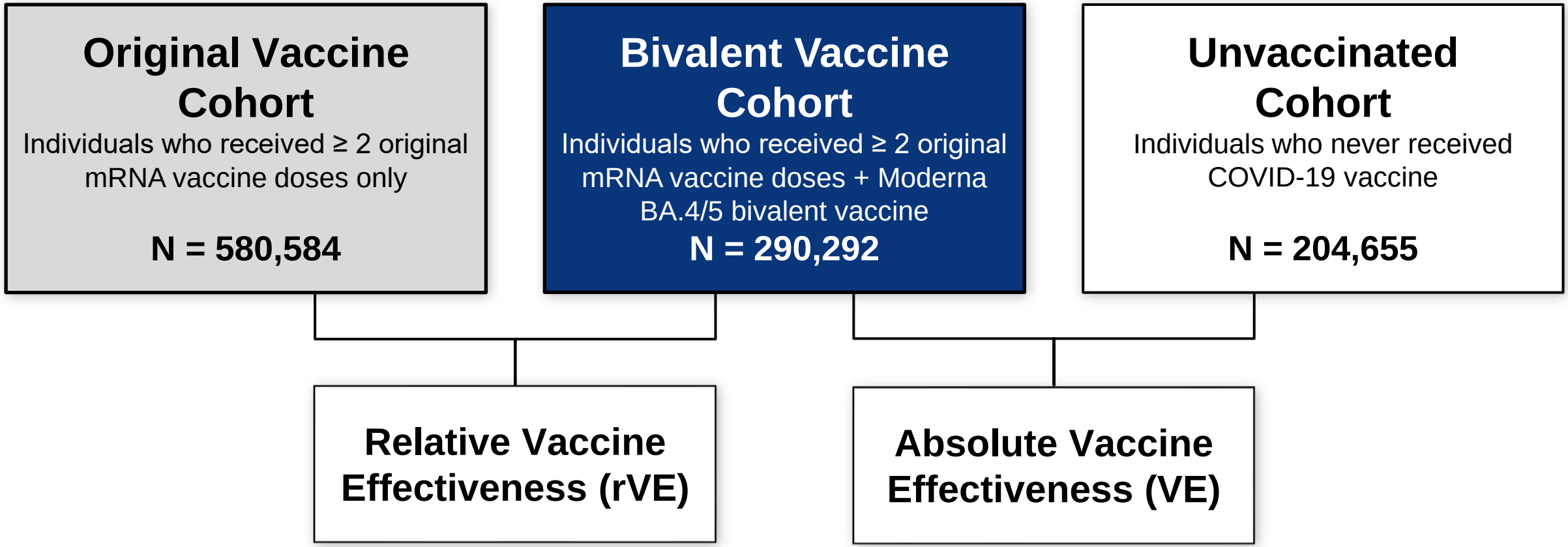
Study Period

- Moderna BA.4/5 bivalent vaccine administered 8/31/2022-12/31/2022
- Follow-up through 1/31/2023

Index date for bivalent booster group: Date of receipt of bivalent dose
Index date for monovalent & unvaccinated groups: Date assigned to match bivalent booster group within age/sex/race risk set
Tseng et al., *MedRxiv,* 2023

Comparisons for Vaccine Effectiveness

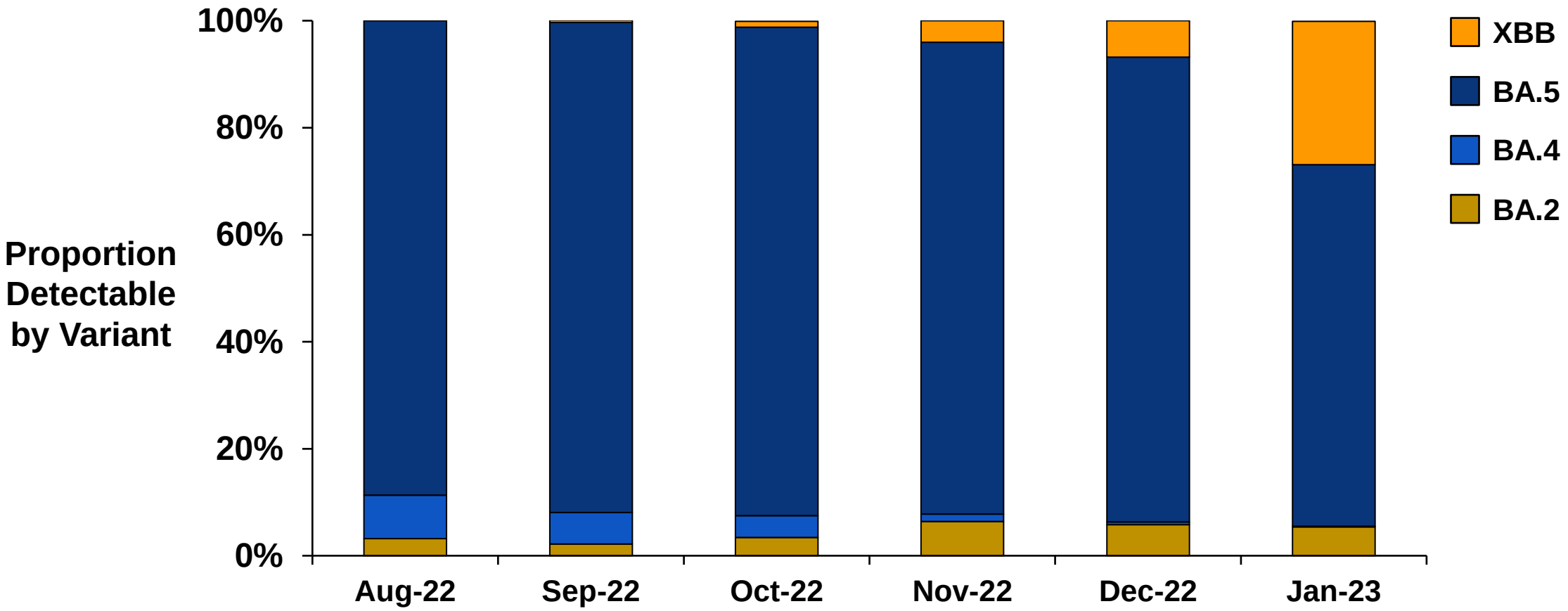
Study 901 - Kaiser Permanente Southern California Effectiveness Study



Tseng et al., *MedRxiv,* 2023

SARS-CoV-2 Variant Distribution, Aug 2022 – Jan 2023 (N = 26,993 samples)

Study 901 - Kaiser Permanente Southern California Effectiveness Study



Kaiser – unpublished data
71% of XBB isolates in Jan 2023 were XBB.1.5

Study Population - Baseline Characteristics
Aug 31, 2022 – Jan 31, 2023

Study 901 - Kaiser Permanente Southern California Effectiveness Study

Baseline Characteristic	Original Vaccine Cohort N = 580,584	Moderna BA.4/5 Bivalent Cohort N = 290,292	Unvaccinated Cohort N = 204,655
Median Age – Years (Q1, Q3)	61 (46, 72)	62 (46, 72)	53 (40, 66)
Non-White Race	61%	61%	58%
Number of Original mRNA vaccine doses prior to index date			
2 doses	24%	5%	N/A
3 doses	49%	49%	N/A
≥ 4 doses	27%	46%	N/A
Median Days (Q1, Q3) since last non-bivalent vaccine dose	312 (189, 384)	260 (173, 343)	N/A

Tseng et al., *MedRxiv,* 2023
N/A – not applicable

Effectiveness of Moderna BA.4/5 Bivalent mRNA Vaccine Aug 31, 2022 – Jan 31, 2023

Study 901 - Kaiser Permanente Southern California Effectiveness Study

COVID-19 Outcomes	Relative Vaccine Effectiveness (compared with individuals who had ≥2 original vaccine doses) N = 290,292 bivalent receipts & 580,584 controls	Absolute Vaccine Effectiveness (compared with individuals not vaccinated with any COVID-19 vaccine) N = 290,292 bivalent receipts & 204,655 controls
Hospitalization (Chart confirmed)	**70%** (64%, 75%)	**83%** (79%, 86%)
COVID-19 In-Hospital Deaths	**83%** (64%, 92%)	**90%** (78%, 95%)
ED and Urgent Care	**55%** (51%, 59%)	**55%** (50%, 60%)

Bivalent BA.4/5 booster provides additional protection against hospitalizations, ED, and urgent care visits

Vaccine effectiveness adjusted for demographics, clinical factors/medical conditions, evidence of prior SARS-CoV-2 infection, and/or health-seeking behaviors

Tseng et al., *MedRxiv,* 2023

Variant Monitoring, Risk Assessment, and Preclinical Assessment of Investigational New Variant Vaccines

Darin Edwards, PhD

Executive Director

COVID-19 Program Lead

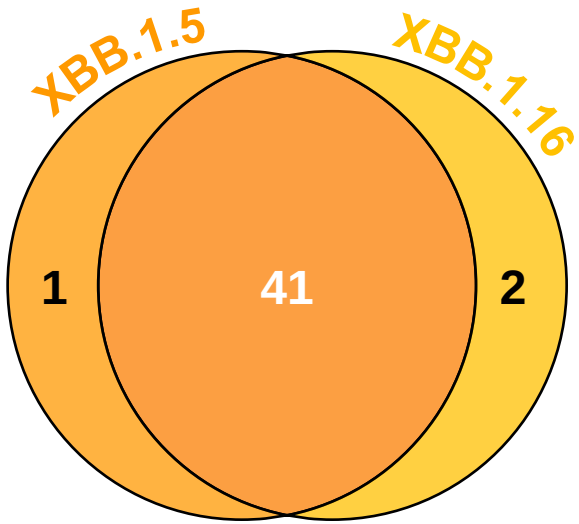
Moderna, Inc.

Moderna Continuously Prepares New Candidate Vaccines Against Emerging Variants

- Continuous epidemiological monitoring and risk assessment of variants
  - Identify variants that contain immune evading mutations versus authorized vaccines and increased growth dynamics regionally or globally
  - Group antigenically similar sub-lineages in our selection (sub-family matching)
  - Select variants for further study based on global and regional coverage
- At-risk candidate vaccine manufacturing preparation and preclinical evaluations begin in parallel
- These activities allow for expedited delivery of updated vaccines, if requested
- XBB sublineage is dominant globally
  - Now focused our efforts on XBB-containing vaccines

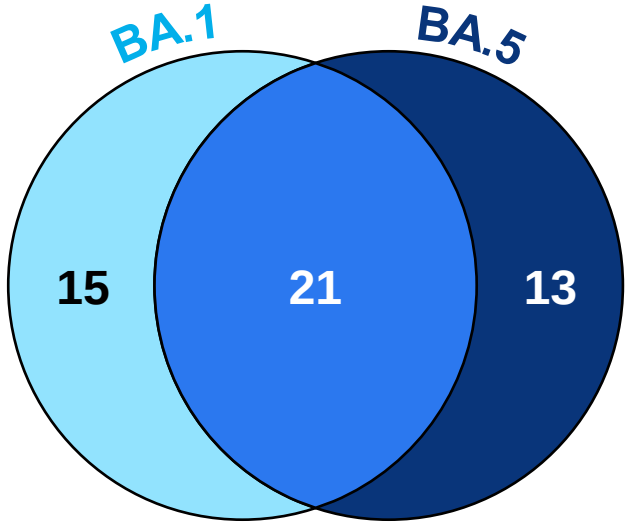
Antigenic Differences Between Variants Drive Selection Strategy

XBB.1.5 vs. XBB.1.16
(Current)



1 + 2 = 3 mutations

BA.1 vs. BA.5
(Past)



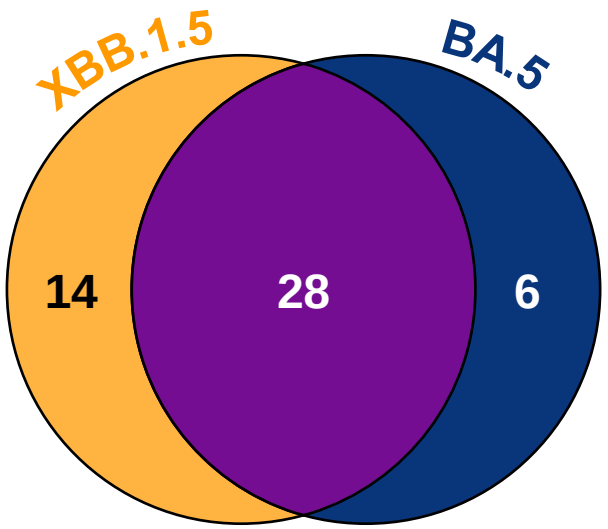
15 + 13 = 28 mutations

- More unique spike mutations when comparing BA.1 and BA.5 than XBB.1.5 and XBB.1.16
- Analysis provides further support to grouping variants into “sub-families” where antigenic distance is minimal and not predicted to be impactful
- BA.1 and BA.5 would NOT have been grouped together into a common sub-family

Venn diagrams generated via cov-spectrum
XBB.1.5 and XBB.1.9.1 have the same spike proteins

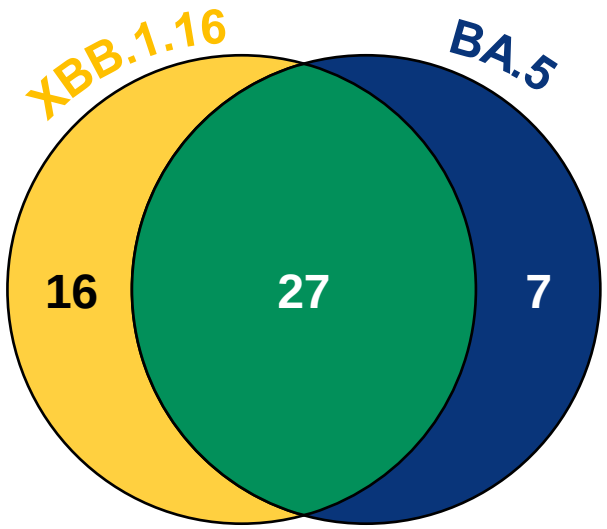
XBB Subvariants Have Significant Antigenic Differences Compared to BA.5 Variant

XBB.1.5 vs. BA.5



14 + 6 = 20 mutations

XBB.1.16 vs. BA.5



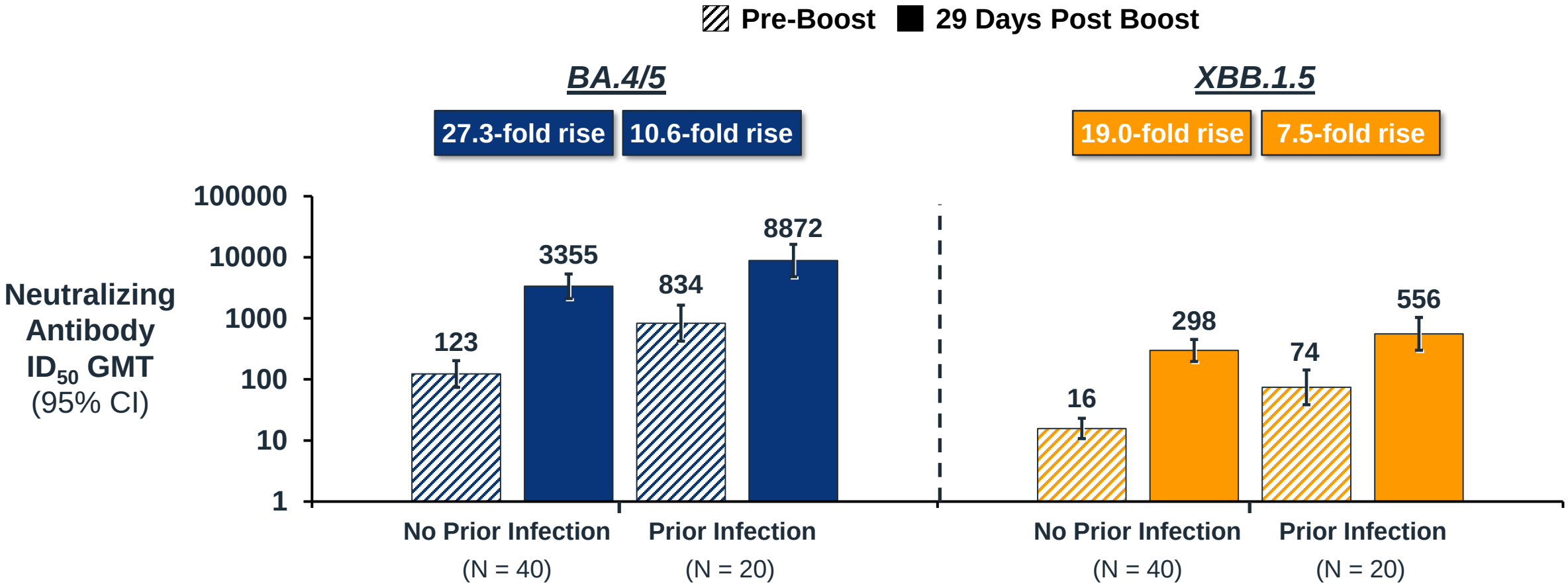
16 + 7 = 23 mutations

Antigenic differences between XBB subvariants and BA.5 suggest an updated vaccine composition may be needed

Venn diagrams generated via cov-spectrum
XBB.1.5 and XBB.1.9.1 have the same spike proteins

Cross-Neutralization at Day 29 Following Omicron BA.4/5 Bivalent Booster

Study 205H, Per-Protocol Immunogenicity Set

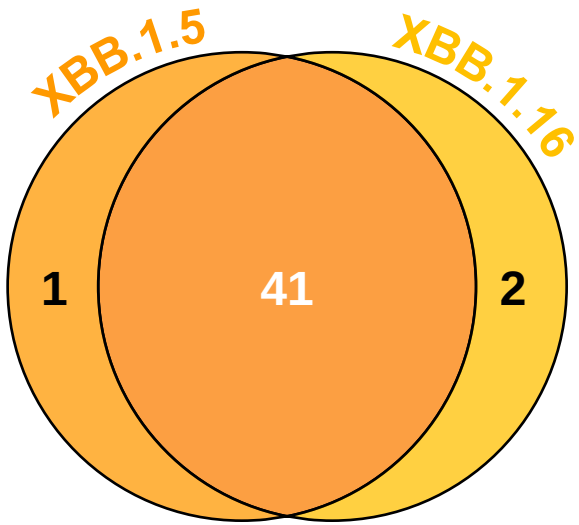


Neutralization capacity of currently authorized BA.4/5 vaccine considerably less against XBB.1.5

Chalkias et al., *medRxiv*, 2022

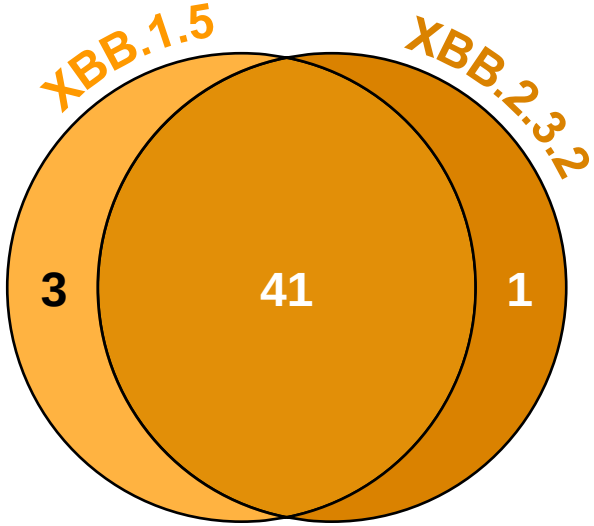
Minimal Antigenic Differences Between Circulating XBB Variants (XBB.1.5, XBB.1.16, and XBB.2.3.2)

XBB.1.5 vs. XBB.1.16



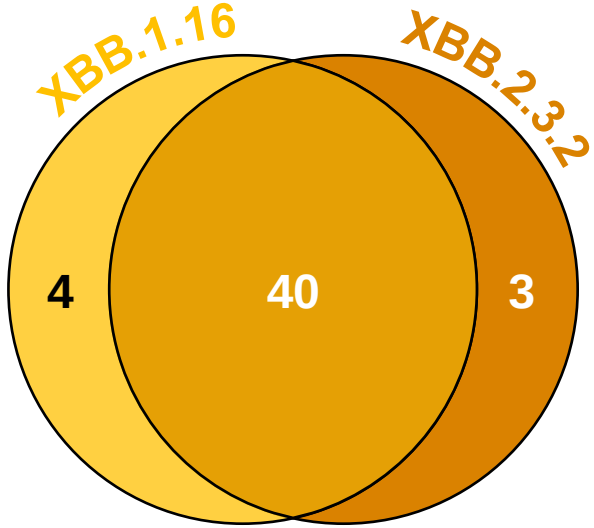
1 + 2 = 3 mutations

XBB.1.5 vs. XBB.2.3.2



3 + 1 = 4 mutations

XBB.1.16 vs. XBB.2.3.2



4 + 3 = 7 mutations

XBB-containing vaccines will likely perform similarly; cross-neutralization is unlikely to be significantly impacted

Venn diagrams generated via cov-spectrum
XBB.1.5 and XBB.1.9.1 have the same spike proteins

Overview of Preclinical Studies to Assess Investigational XBB-Containing Vaccines

Preclinical Studies Conducted with XBB.1.5 and XBB.1.16-Containing Vaccine Candidates

Studies to compare investigational XBB sub-variant containing vaccine formulations in mice:

Primary Series

Antigen naïve mice

Monovalent and Bivalent XBB.1.5-Containing Vaccines
Complete

Monovalent and Bivalent XBB.1.16-Containing Vaccine
Ongoing

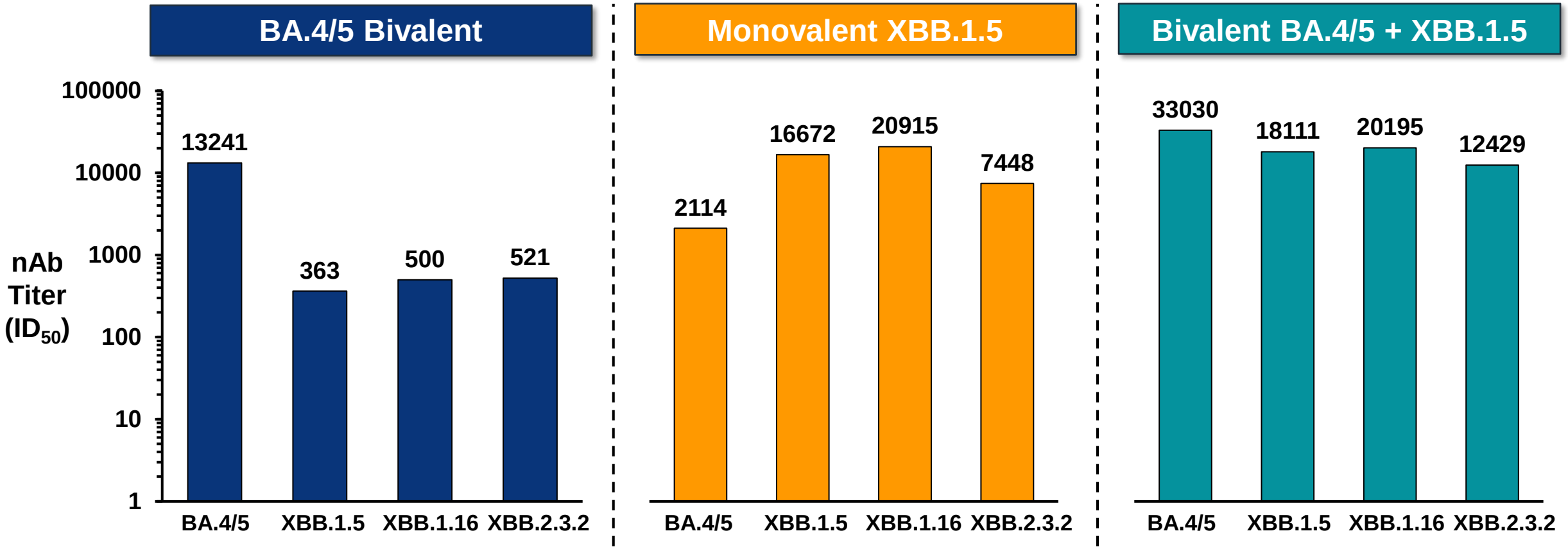
Booster (3rd) Dose

Mice previously immunized with a 2-dose primary series of mRNA-1273

Monovalent and Bivalent XBB.1.5-Containing Vaccines
Complete

Monovalent and Bivalent XBB.1.16-Containing Vaccines
Complete

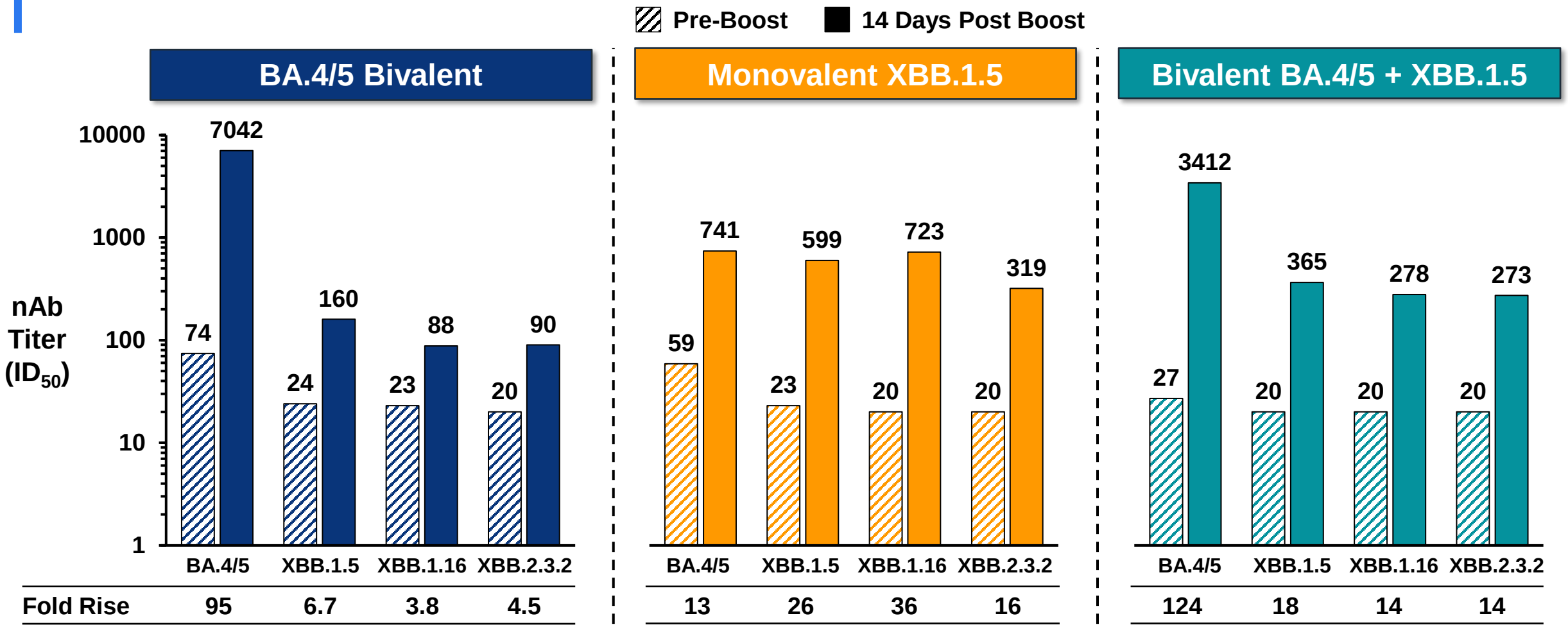
Neutralizing Antibody Titers in Mice 14 Days after Primary Series of XBB.1.5-Containing Vaccines



Monovalent and bivalent XBB.1.5-containing vaccines effectively drive neutralization of XBB subvariant viruses

1µg dose, D1 and D22, n=8 per group

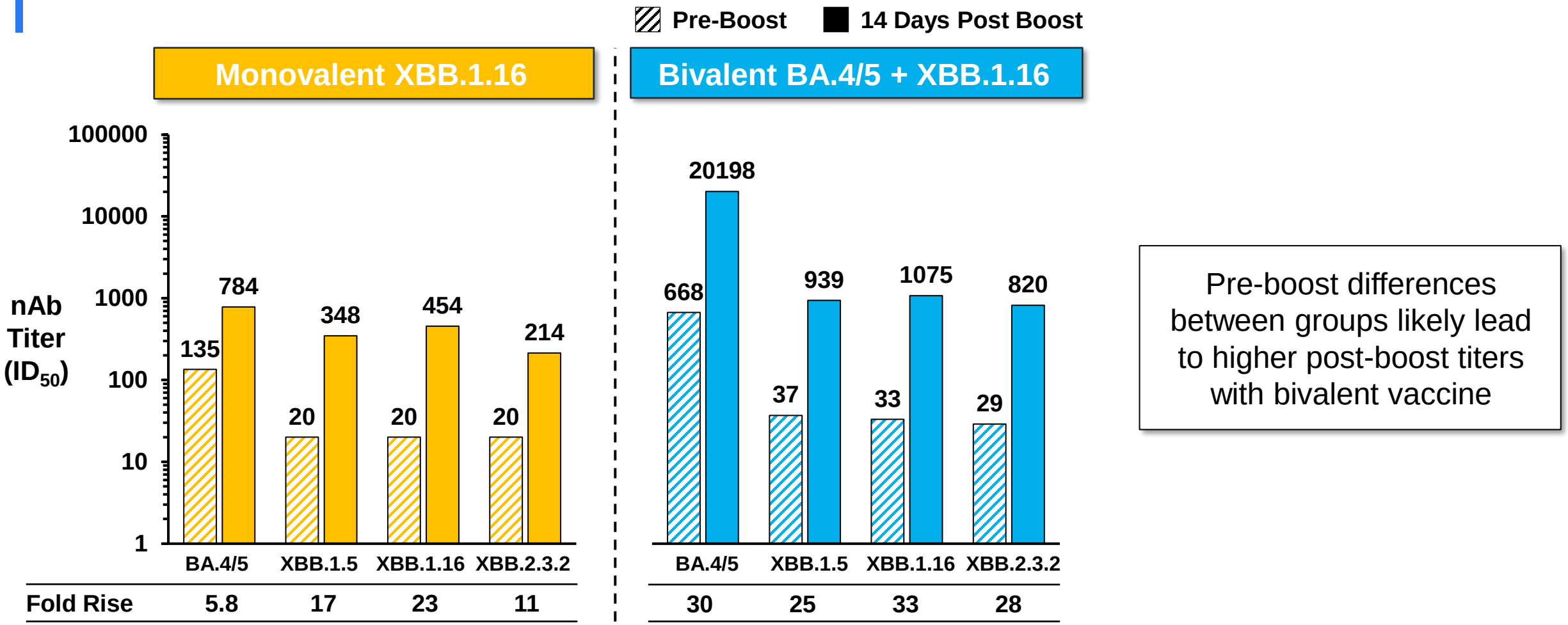
Neutralizing Antibody Titers in Mice 14 Days after Booster (3rd) Dose of XBB.1.5-Containing Vaccines



Monovalent and bivalent XBB.1.5-containing vaccines effectively increase neutralization of XBB sub-variant viruses

0.5 µg dose, D1 and D22; 1 µg D91, n=8 per group

Neutralizing Antibody Titers in Mice 14 Days after Booster (3rd) Dose of XBB.1.16-Containing Vaccines



Pre-boost differences between groups likely lead to higher post-boost titers with bivalent vaccine

Monovalent and bivalent XBB.1.16 containing vaccines effectively increase neutralization of XBB sub-variant viruses

0.5 µg dose, D1 and D22; 1 µg D69, n=8 per group

Summary of Pre-Clinical Data

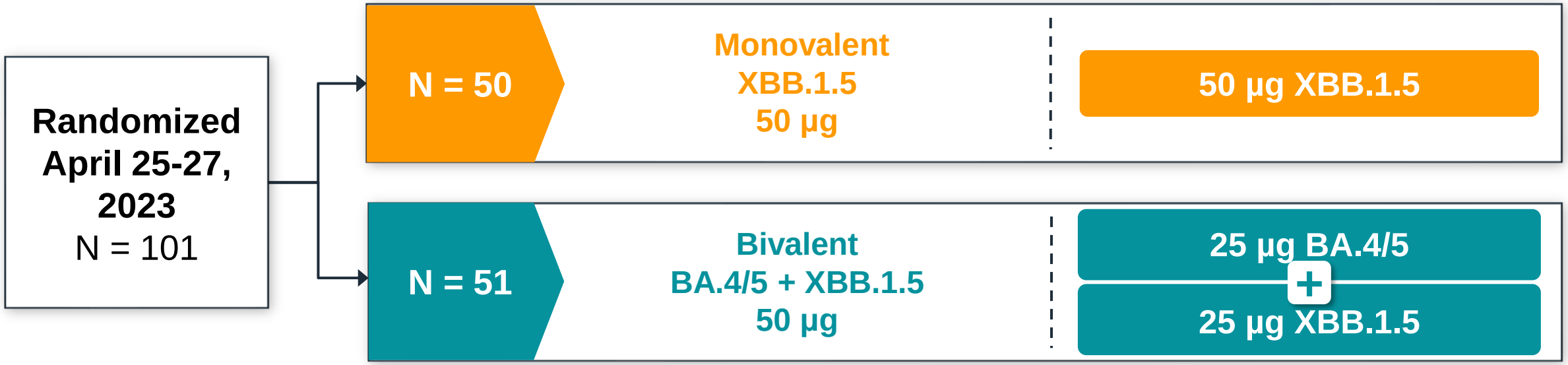
- Preclinical data suggest that an XBB-containing vaccine is more immunogenic against currently circulating XBB variants
- Minimal antigenic differences seen across the XBB sub-family
- Cross-neutralization across XBB sub lineage for both XBB-containing vaccines was demonstrated

Clinical Trial of Investigational XBB.1.5 Variant-Containing Vaccines

Rituparna Das, MD, PhD

Phase 2/3 Randomized Safety and Immunogenicity Study of XBB.1.5-Containing Booster in Adults ≥18 Years

Study 205J, 5th Dose (3rd Booster)



- All participants previously received 4 doses of vaccine:
  - Original vaccine primary series + booster
  - Any mRNA BA.4/5 booster ≥3 months prior to enrollment
- All analyses are descriptive

https://clinicaltrials.gov/ct2/show/NCT04927065

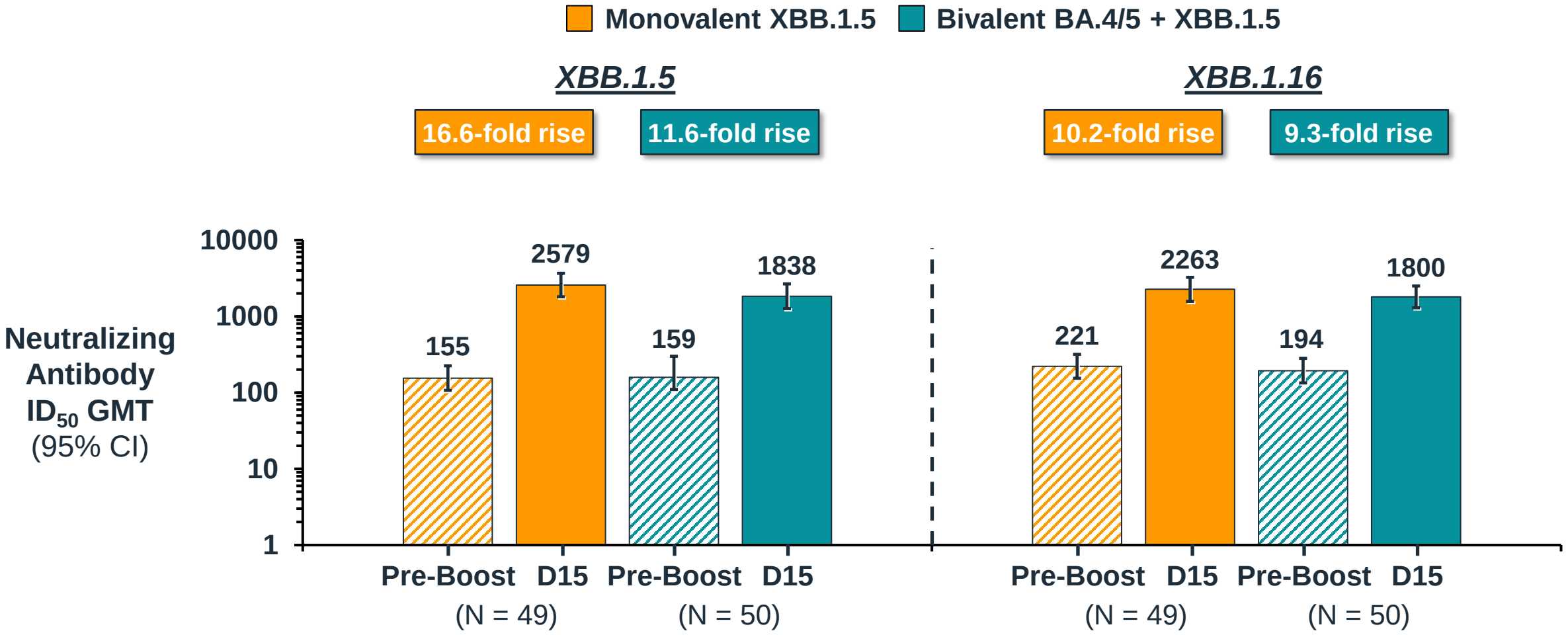
Demographics and Baseline Characteristics

Study 205J, 5th Dose (3rd Booster)

Characteristic	5th Dose (3rd Booster)	
	Monovalent XBB.1.5 N = 50	Bivalent BA.4/5 + XBB.1.5 N = 51
Mean Age – Years	51.6	48.4
Median Age – Years (range)	55 (21, 84)	48 (24, 82)
≥ 65 years	11 (22.0%)	7 (13.7%)
% Female	30 (60.0%)	31 (60.8%)
Non-White Race	5 (10.0%)	10 (19.6%)
Months between 2nd and 3rd Dose, median (Q1, Q3)	8.2 (7.8, 9.8)	9.2 (7.8, 12.2)
Months between 3rd and 4th Dose, median (Q1, Q3)	9.8 (8.3, 10.3)	9.2 (8.2, 10.3)
Months between 4th and 5th Dose, median (Q1, Q3)	8.2 (8.1, 8.3)	8.3 (8.1, 8.4)
Prior SARS-CoV-2 Infection	34 (68.0%)	40 (78.4%)

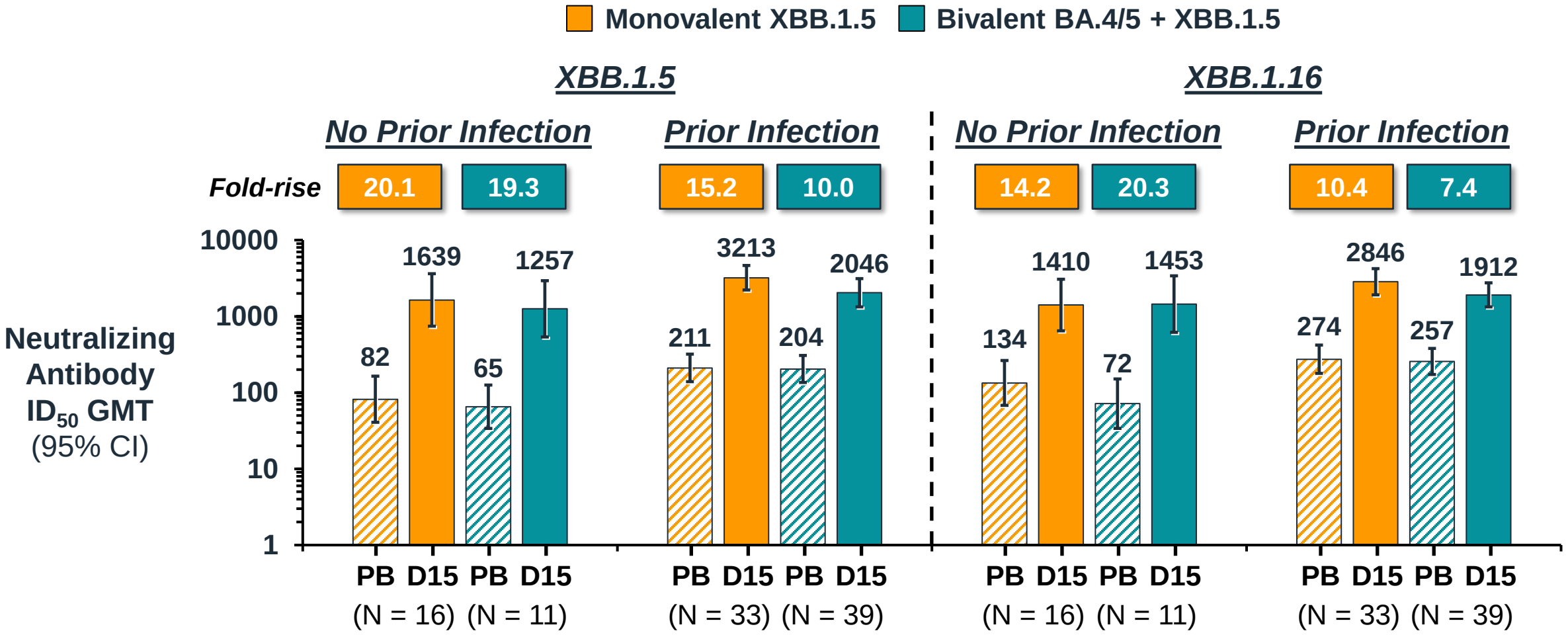
XBB.1.5 and XBB.1.16 Neutralizing Antibodies After 5th Dose (3rd Booster) of XBB-Containing Vaccines in Adults

Study 205J, Per-Protocol Immunogenicity Set – All Participants



XBB.1.5 and XBB.1.16 Neutralizing Antibodies After 5th Dose (3rd Booster) of XBB-Containing Vaccines in Adults

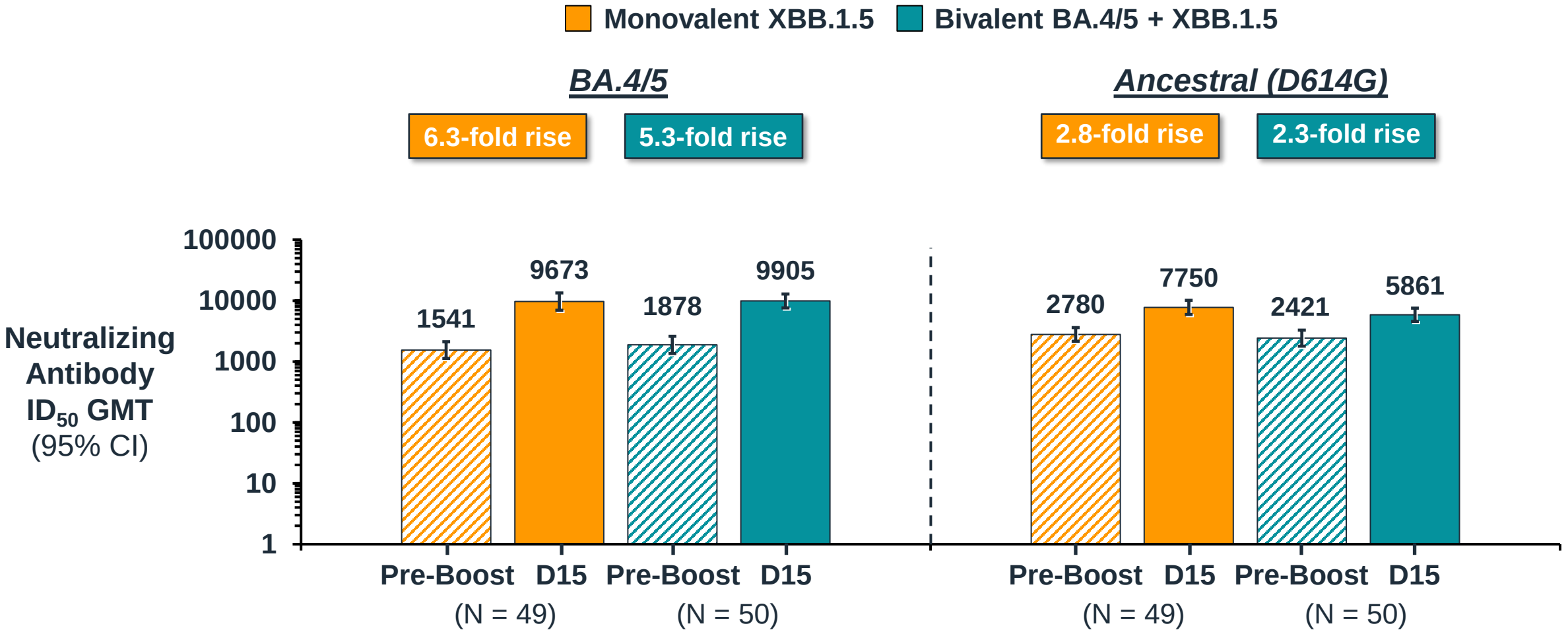
Study 205J, Per-Protocol Immunogenicity Set – By Prior Infection Status



PB = Pre-Boost

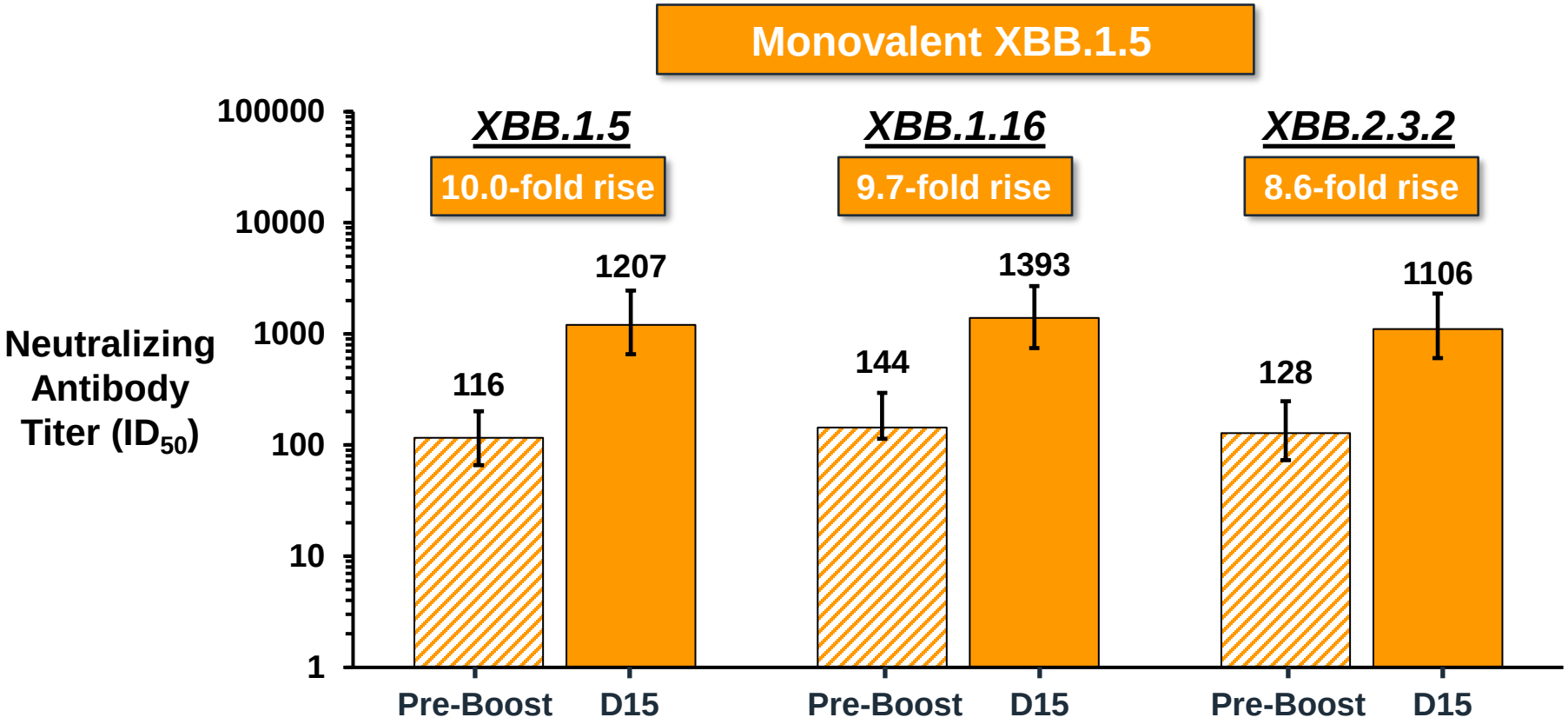
BA.4/5 and Ancestral (D614G) Neutralizing Antibodies After 5th Dose (3rd Booster) of XBB-Containing Vaccines in Adults

Study 205J, Per-Protocol Immunogenicity Set – All Participants



XBB.1.5, XBB.1.16, and XBB.2.3.2 Neutralizing Antibodies After 5th Dose (3rd Booster) of Monovalent XBB.1.5 Vaccine in Adults

Study 205J, Subset Analysis (N = 20)

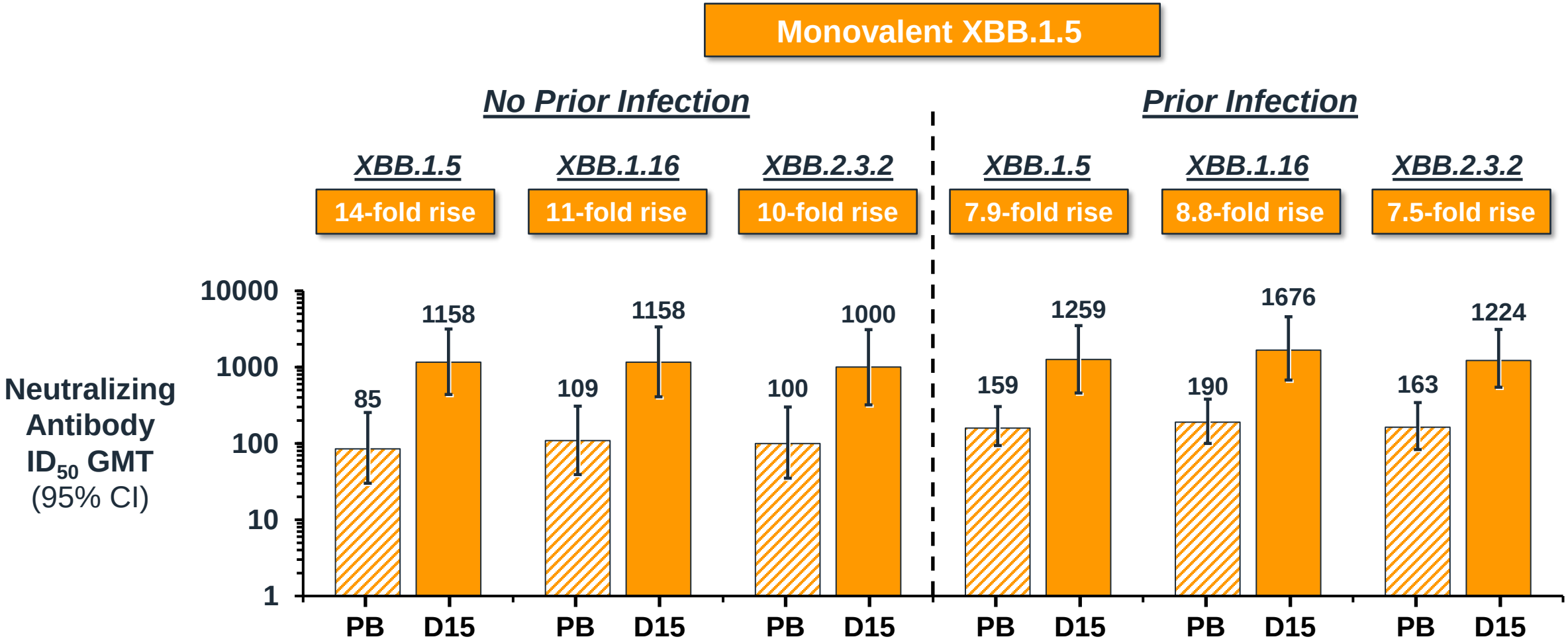


Similar neutralization of XBB.1.5, XBB.1.16, and XBB.2.3.2 sub-variants measured in this subset analysis

Moderna PSVN research assay

XBB.1.5, XBB.1.16, and XBB.2.3.2 Neutralizing Antibodies After 5th Dose (3rd Booster) of XBB-Containing Vaccines in Adults

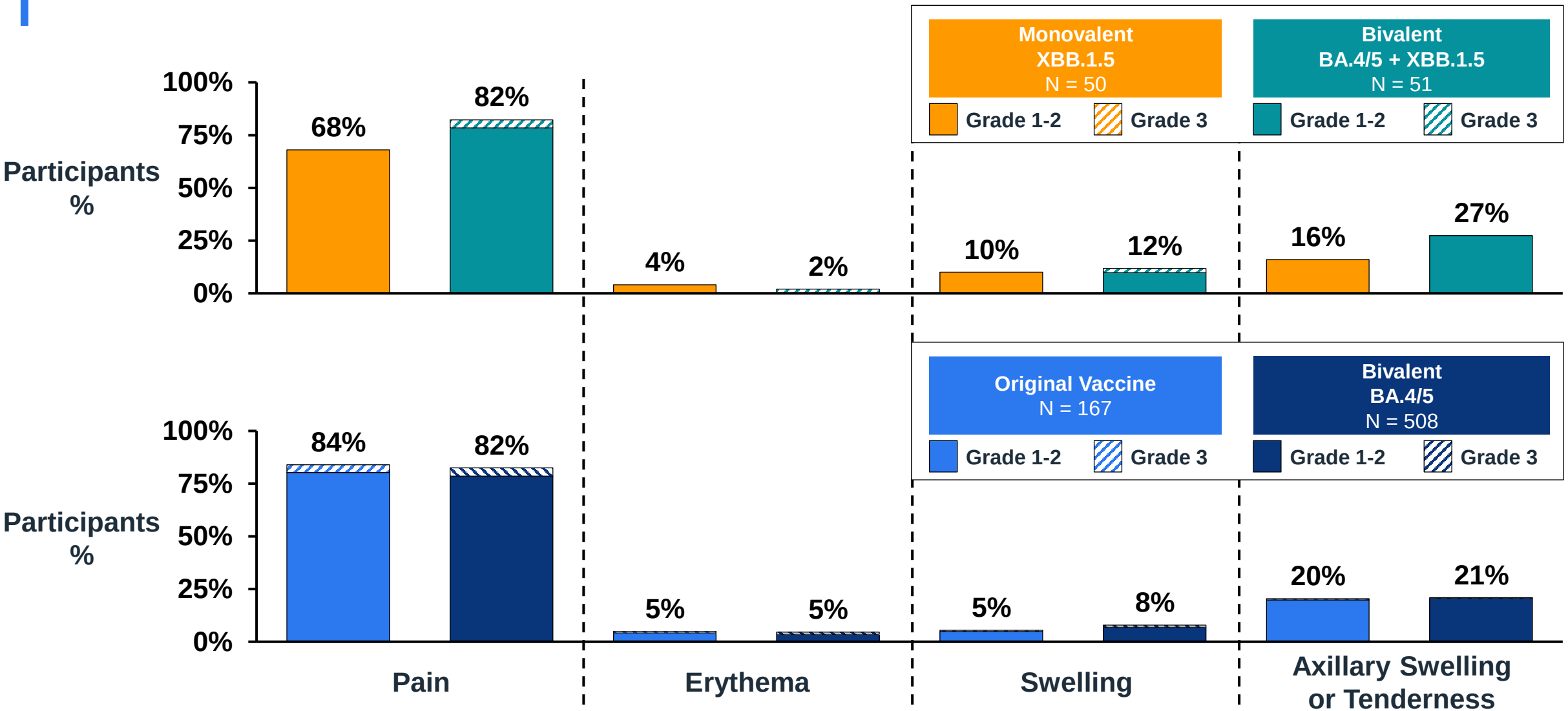
Study 205J, Subset Analysis (N=10 With Prior Infection, N=10 Without Prior Infection)



PB = Pre-Boost

Local Reactions Following Booster Doses in Adults

Study 205J and Study 205H, Solicited Safety Set

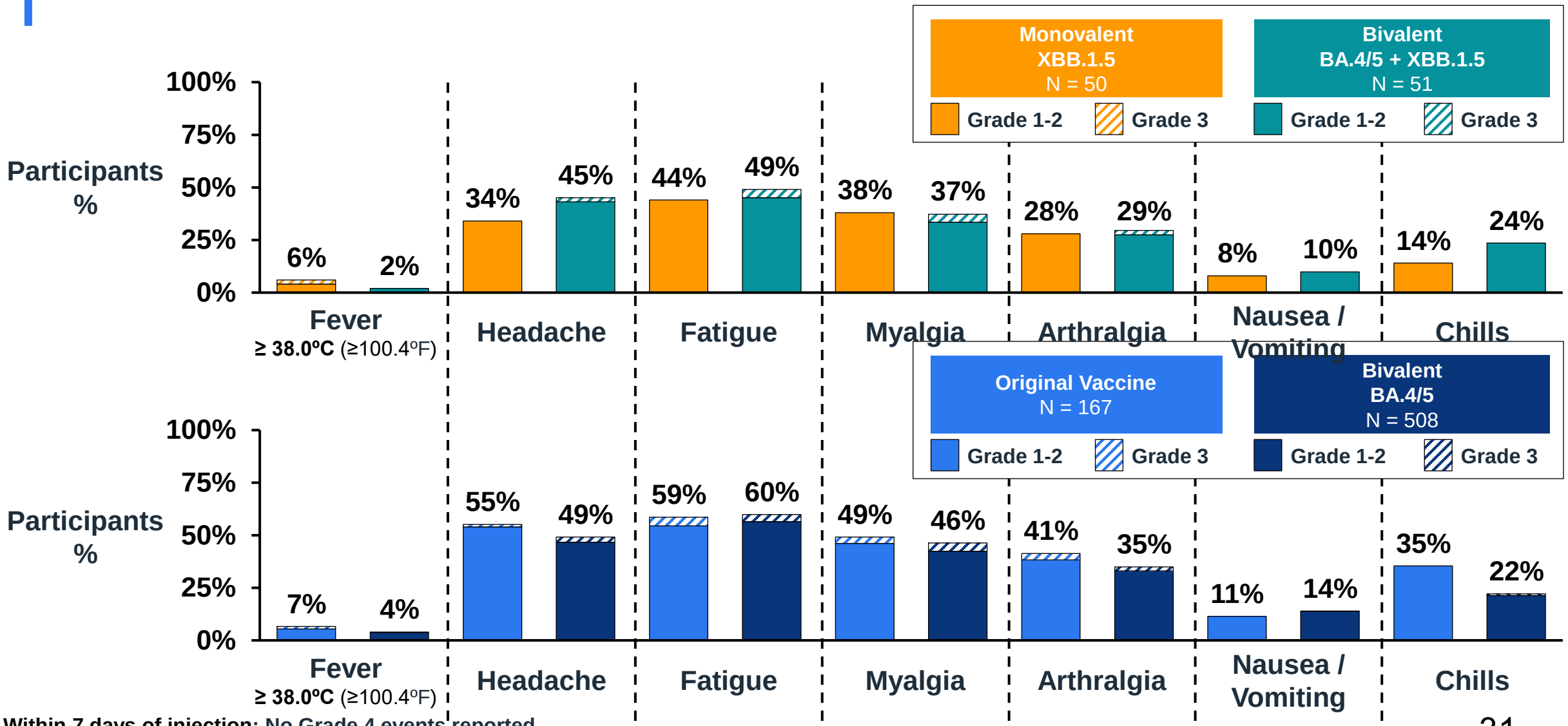


Within 7 days of injection; No Grade 4 events reported

Chalkias et al., ***medRxiv,*** **2022**, Chu et al, ***Nat Med*** **28:1041, 2022**

Systemic Reactions Following Booster Doses in Adults

Study 205J and Study 205H, Solicited Safety Set



Within 7 days of injection; No Grade 4 events reported

Chalkias et al., *medRxiv,* 2022, Chu et al, *Nat Med* 28:1041, 2022

Conclusions

Rituparna Das, MD, PhD

Summary

Kaiser Real World Effectiveness Study	▪ BA.4/5 booster effective against COVID-19 when BA.5 was the predominant circulating strain
Preclinical and Clinical Studies of XBB-containing Vaccines	▪ Antigenic similarities in XBB-variants support grouping of the XBB viruses ▪ Pre-clinical data suggest an XBB-containing vaccine is more immunogenic against currently circulating XBB variants than the authorized BA.4/5 vaccine ▪ Clinical data demonstrate that XBB.1.5-containing vaccines robustly elicit neutralizing antibodies against XBB variants ▪ Safety profile of XBB-containing vaccines consistent with previously authorized vaccines
Moderna's Vaccine Preparedness	▪ Moderna is prepared to supply a new variant-containing vaccine for Fall 2023 as recommended by FDA

THANK YOU to Our Study Collaborators, Investigators, and Participants

- All investigators
- Study site personnel
- Most importantly, the individuals who participated in these trials

2023-2024 COVID-19 Vaccine Formula: Pfizer/BioNTech Clinical and Preclinical Supportive Data

Vaccines and Related Biological Products Advisory Committee

June 15, 2023

Presentation Outline

Kena A. Swanson, Ph.D.
Vice President, Viral Vaccines
Vaccine Research and Development, Pfizer Inc.

Epidemiology & Real-World Evidence

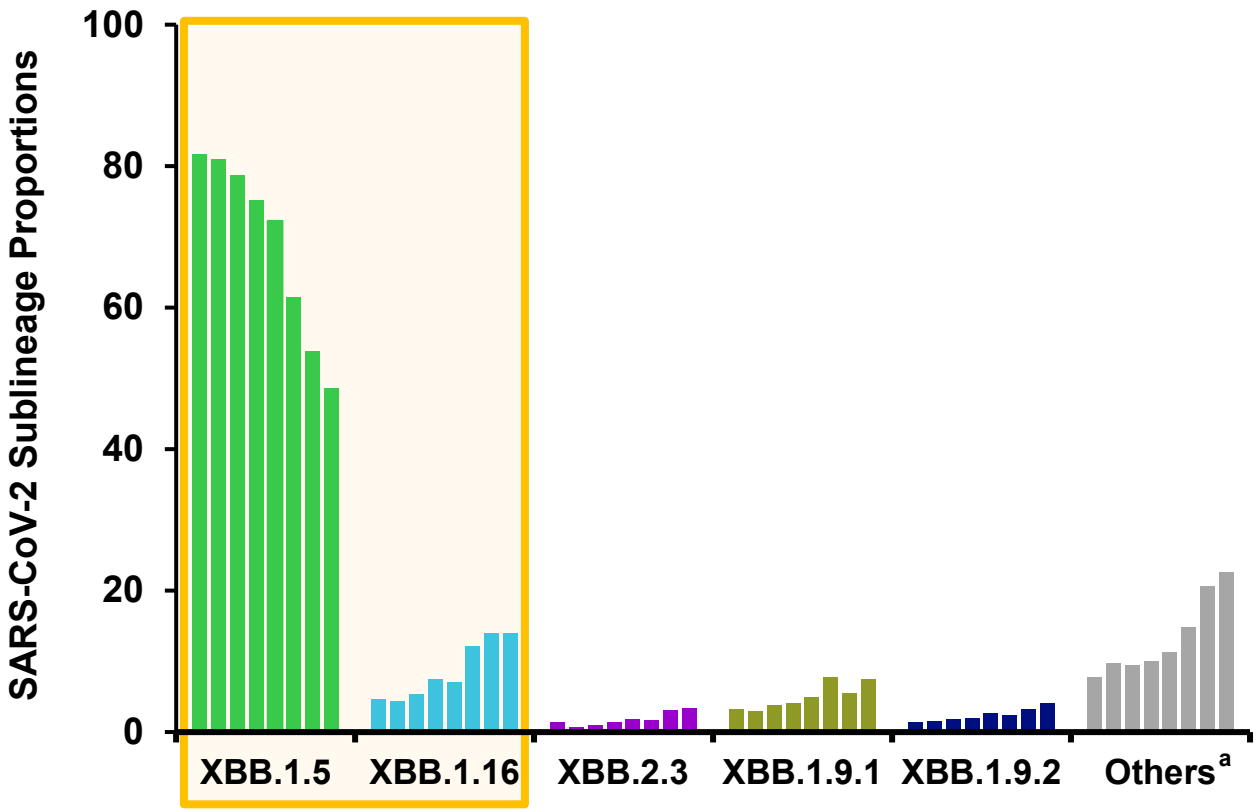
Omicron-Adapted Vaccine Booster Dose Humoral and Cell-Mediated Immune Responses

Preclinical Evaluation Against Contemporary Variant Vaccines

Supply of 2023-2024 Formula

The Current COVID-19 Epidemiologic Landscape in the US is Dominated by XBB.1.5 and Related Sublineages

Weekly Proportions from 1-Apr to 20-May



Circulating XBB Sublineages are Similar

- **XBB.1.9.1 and XBB.1.9.2**: same spike amino acid sequence as XBB.1.5
- **XBB.1.16**: differs from XBB.1.5 at two spike amino acid residues
- **XBB.2.3**: differs from XBB.1.5 at three spike amino acid residues

GISAID, data accessed as of June 4, 2023
XBB.1.5, XBB.1.16, XBB.2.3, XBB.1.9.1, XBB.1.9.2 sublineage categories include descendants that have no amino acid differences in spike protein from parental sublineage.
a. Others include: XBB.1.16.1, EU.1.1.1, FL.4, FD.2, XBB.1.5.1 (sublineages that exceed a threshold of 1.8% in any week).

Waning Effectiveness of Current Bivalent Vaccines Against XBB Sublineages

Rationale for Fall Vaccine Update

- XBB sublineages dominant globally and antigenically distant from prior Omicron strains[1,2]
- Current bivalent vaccines maintain effectiveness[3-11] but show signs of waning, including against severe COVID-19[3,9-11]
- Immunity likely further reduced by fall
- Better-matched vaccines improve protection[3]

Absolute VE Against Hospitalization, CDC[11]

Immunocompetent Adults, VISION Network, Sep 2022 – Apr 2023

	Time Since mRNA Vaccination	Adjusted VE (95% CI)
Age 18–64y	Monovalent only, ≥7 days*	17 (7–26)
	Bivalent booster, 7–59 days	61 (44–72)
	Bivalent booster, 60–119 days	25 (1–43)
	Bivalent booster, 120–179 days	16 (-24–43)†

* Median (IQR) time since last dose: 403 (306-534) days

† These estimates are imprecise and should be interpreted with caution.

	Time Since mRNA Vaccination	Adjusted VE (95% CI)
Age ≥65y	Monovalent only, ≥7 days*	24 (18–29)
	Bivalent booster, 7–59 days	64 (58–68)
	Bivalent booster, 60–119 days	51 (45–57)
	Bivalent booster, 120–179 days	27 (15–37)

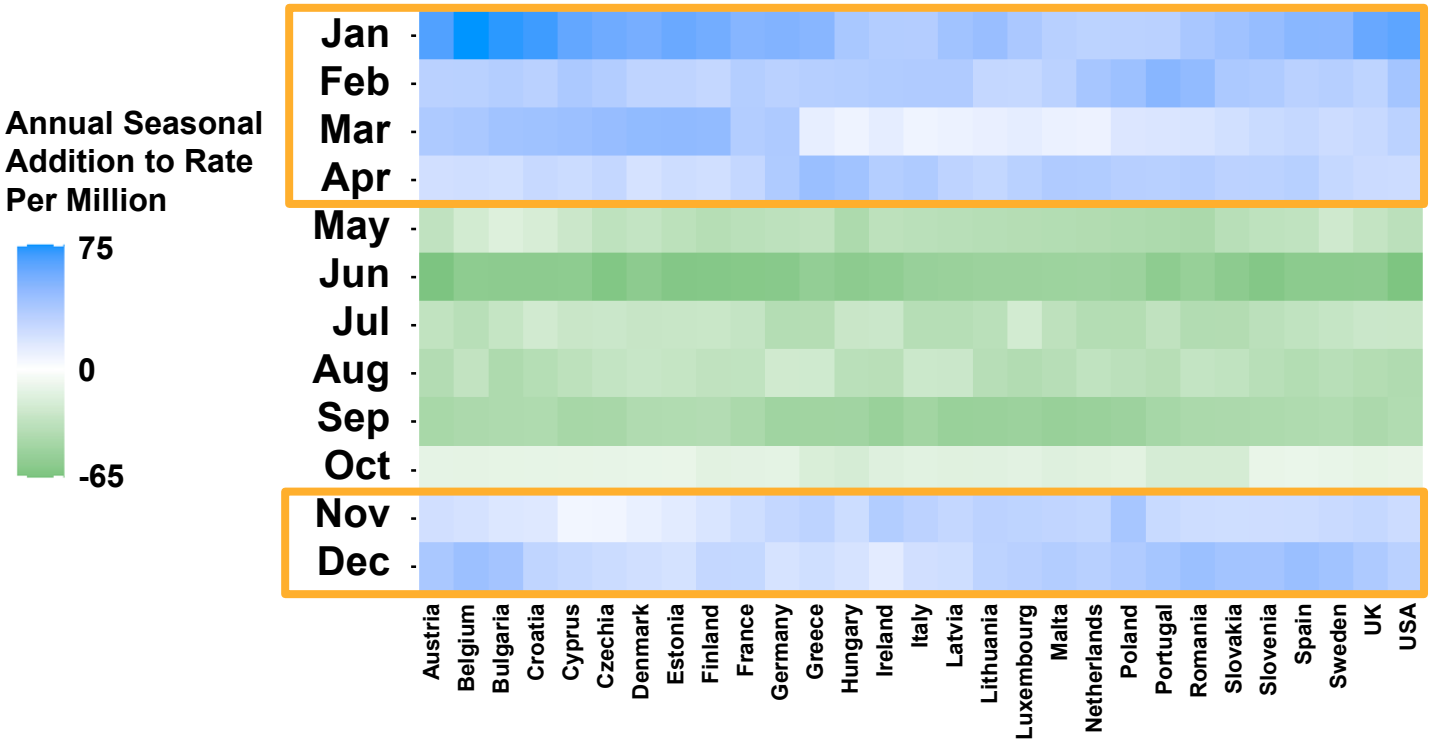
* Median (IQR) time since last dose: 362 (245-484) days

1. World Health Organization. Weekly epidemiological update on COVID-19 - 6 April 2023. Available at: Weekly epidemiological update on COVID-19 - 6 April 2023 (who.int)
2. covSPECTRUM dashboard. Available at: https://cov-spectrum.org/explore/World/AllSamples/Past6M
3. Lin et al. N Engl J Med. 2023 Feb 23;388(8):764-766. doi: 10.1056/NEJMc2215471
4. Link-Gelles et al. MMWR Morb Mortal Wkly Rep 2023;72:119–124. doi: 10.15585/mmwr.mm7205e1
5. Surie et al. MMWR Morb Mortal Wkly Rep 2022;71:1625–1630. DOI: 10.15585/mmwr.mm715152e2
6. Tenforde et al. MMWR Morb Mortal Wkly Rep 2023;71:1637–1646. DOI: 10.15585/mmwr.mm7153a1
7. Fabiani et al. Euro Surveill. 2023 Feb;28(8):2300105. doi: 10.2807/1560-7917.ES.2023.28.8.2300105
8. Tartof et al. Unpublished analysis, under review.
9. Poukka et al. medRxiv 2023. doi: 10.1101/2023.03.02.23286561
10. Link-Gelles R. CDC. Data presented at the ACIP meeting (April 19, 2023). Available at: ACIP meeting (CDC.gov)
11. Link-Gelles R. MMWR Morb Mortal Wkly Rep 2023;72:579–588. DOI: http://dx.doi.org/10.15585/mmwr.mm7221a3

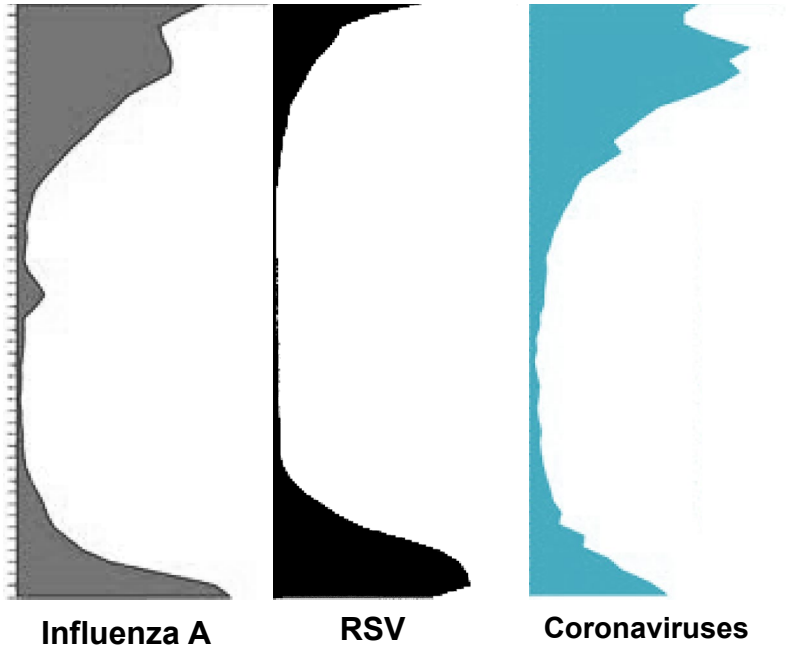
SARS-CoV-2 Activity is Expected to Increase this Autumn/Winter

- **Disease activity has peaked between November and April[1]**
  - Similar to patterns seen for influenza, RSV, and other coronaviruses[2]

Heatmap of Monthly Median COVID-19-Related Hospitalizations Per Million Population, Northern Hemisphere, Mar 2020 – Dec 2022[1]



Weekly Seasonality of Confirmed Viral Infections, England and Wales, 1989 – 2019[2]



1. Wiemken et al. Sci Rep. 2023 Mar 8;13(1):3886. doi: 10.1038/s41598-023-31057-1
2. Nichols et al. BMC Infect Dis. 2021 Oct 26;21(1):1101. doi: 10.1186/s12879-021-06785-2.

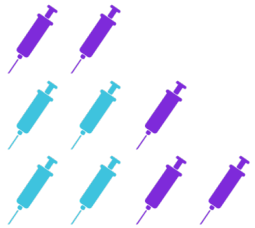
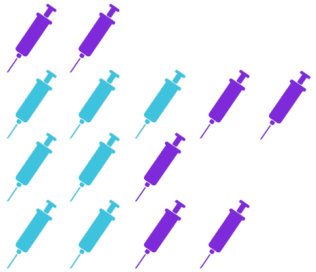
CC-5

Omicron-Adapted Vaccine Booster Dose Humoral and Cell-mediated Immune Responses

Immunogenicity Data From Omicron BA.1 and BA.4/5-adapted Vaccine Clinical Studies Support Real World Evidence Observations

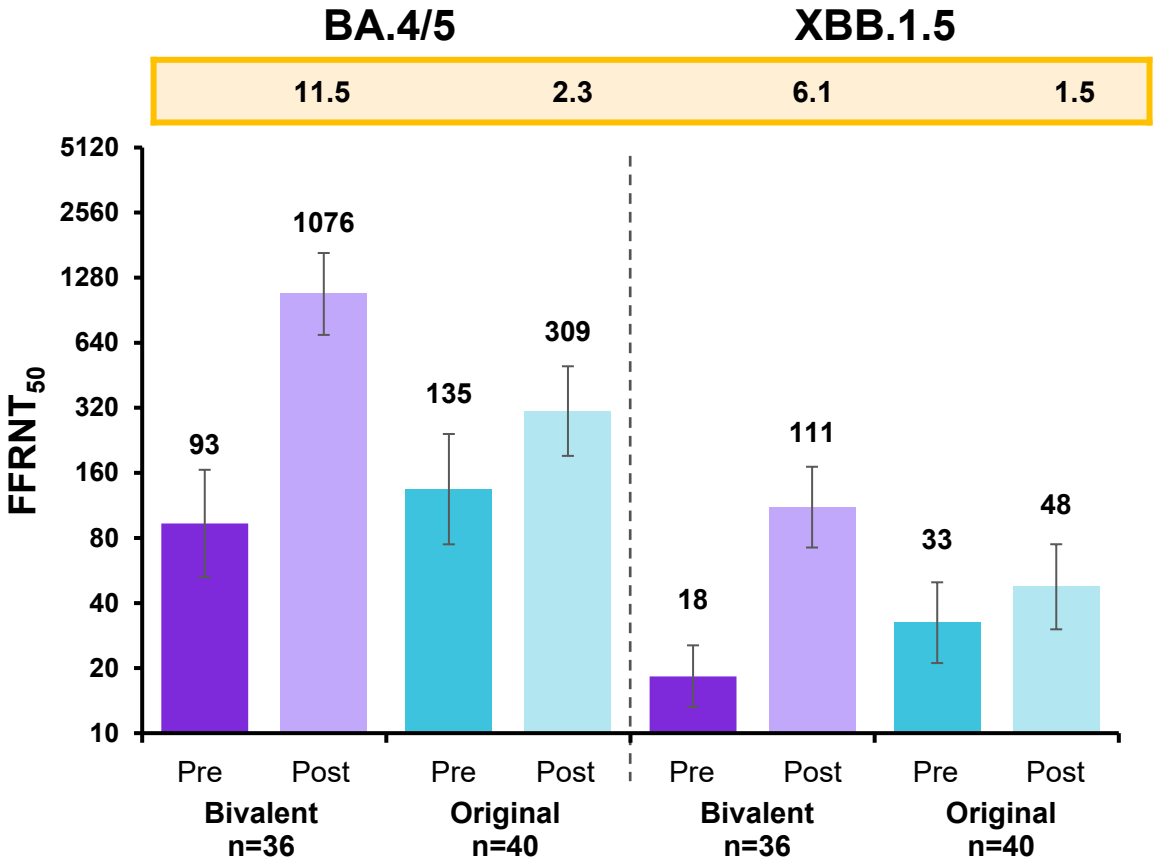
- **Omicron-adapted boosters:**
  - Result in superior variant neutralization titers (NTs) compared to the original vaccine
  - Recall spike-specific memory B cells that recognize shared epitopes; Omicron-specific B cells are also induced
  - Expand spike-specific CD4 and CD8 T cell responses

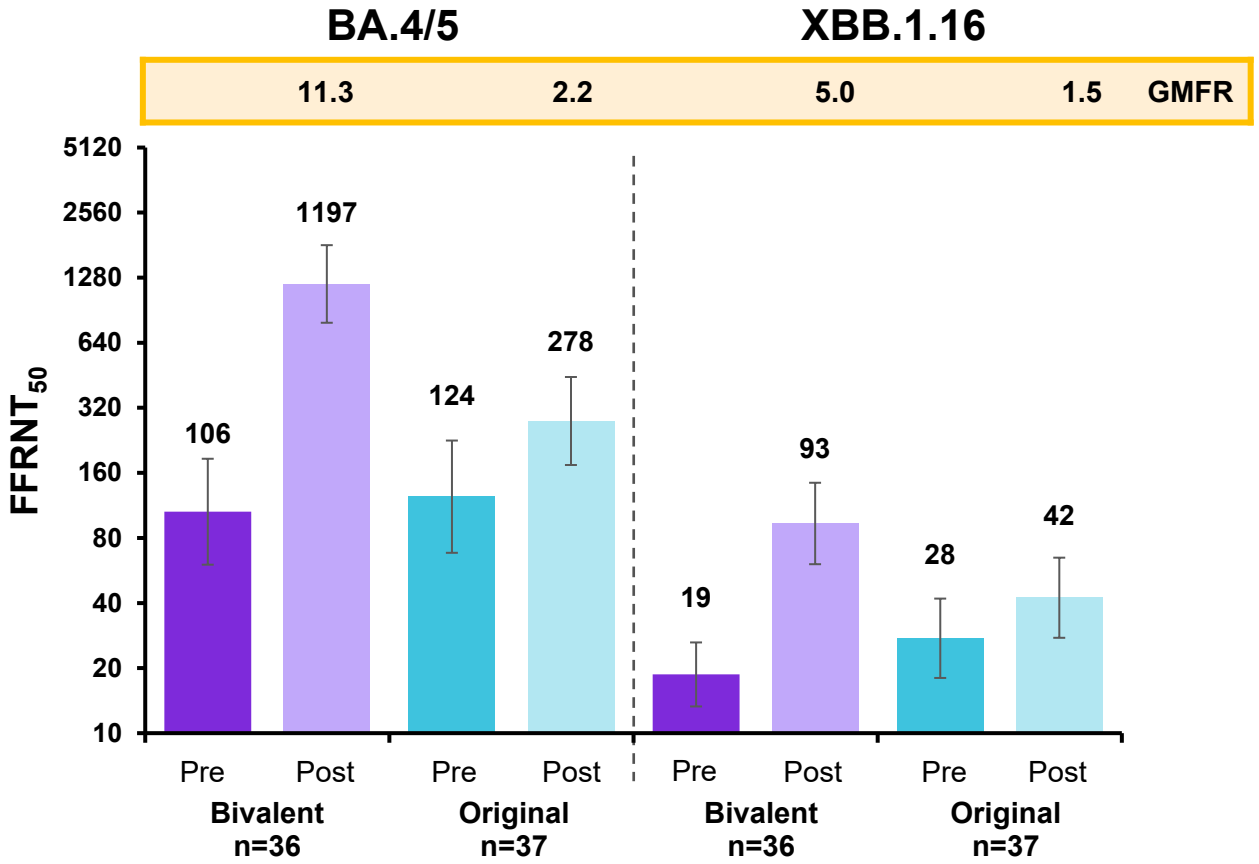
Clinical and Preclinical Experience with Variant-modified Vaccines – Supported Bivalent BA.4/5 Vaccine Authorization

Modified Vaccine	Age Group	Vaccine Regimen	Clinical Data	Preclinical Data
Beta monovalent	**18 to 55 years**		✓ ✓ ✓	✓ ✓ ✓
Omicron BA.1 monovalent	**18 to 55 years**		✓ ✓ ✓ ✓	✓ ✓ ✓ ✓
Omicron BA.1 bivalent	**18 to 55 years** **>55 years**		✓	✓
Omicron BA.4/5 bivalent	**6 months to 11 years** **12 to 55 years** **>55 years**		✓	✓

Bivalent BA.4/5 Boosts Neutralization Activity Against XBB.1.5 and XBB.1.16

Participants >55 years With or Without Prior SARS-CoV-2 Infection at Baseline





Pre = Pre-dose 4; Post = 1-month post dose 4; $FFRNT_{50}$ = 50% fluorescent focus reduction neutralization titers; GMFR = geometric mean fold rises; GMT = geometric means of neutralization titers
The whiskers indicate 95% CI.
Omicron XBB.1.16 and concurrent Omicron BA.4/5 analyses shown on the right of this slide run after Omicron XBB.1.5 and concurrent Omicron BA.4/5 analyses on the left.

CC-9

Spike-Specific Memory B cell (B_{mem}) Assessment After Bivalent Omicron BA.1 Booster Vaccination

BNT162b2
(3 prior doses)

5-12 months

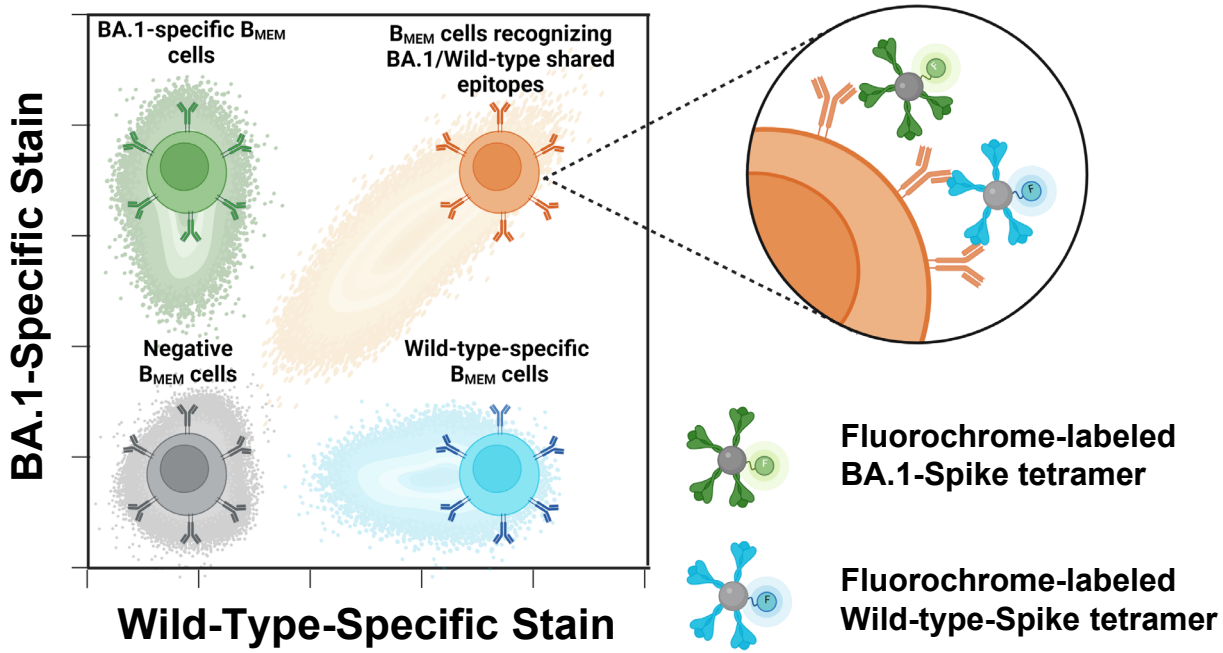
Bivalent BA.1
1-dose booster

WT+Omicron BA.1

>55 years of age

Assessment of Spike-specific Memory B cells

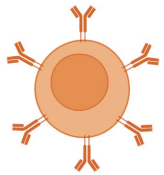
Wild-type strain and Omicron BA.1 Spike protein are used to measure memory B cells recognizing wild-type or Omicron BA.1 exclusive and wild-type/Omicron BA.1 shared epitopes



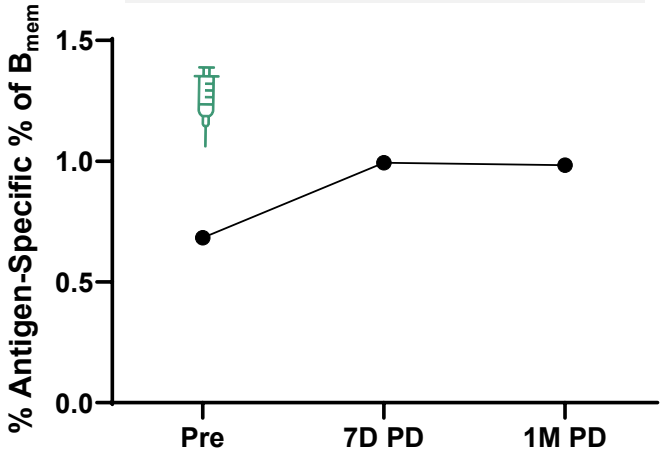
Memory B cells (B_{mem}) defined as CD3−CD19+CD20+IgD−CD38int/low.

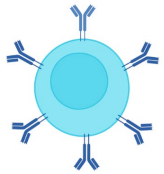
Bivalent Omicron BA.1 Booster Increases the Frequencies of Memory B Cells Recognizing Shared and BA.1-Specific Epitopes

Omicron BA.1 Booster in BNT162b2-experienced Individuals >55 years of Age

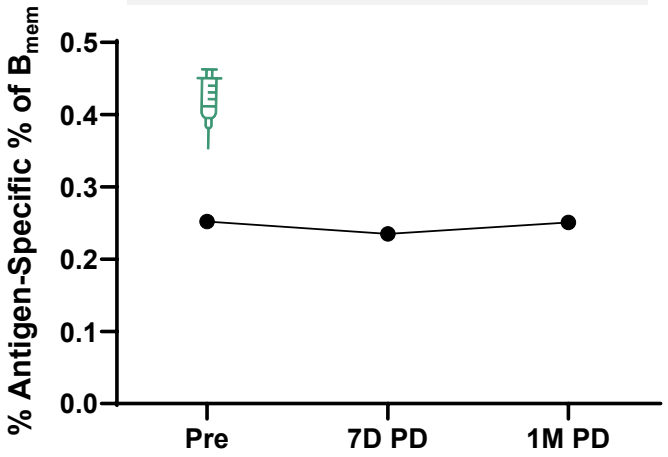


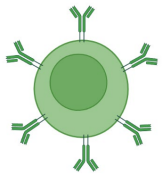
Spike Shared



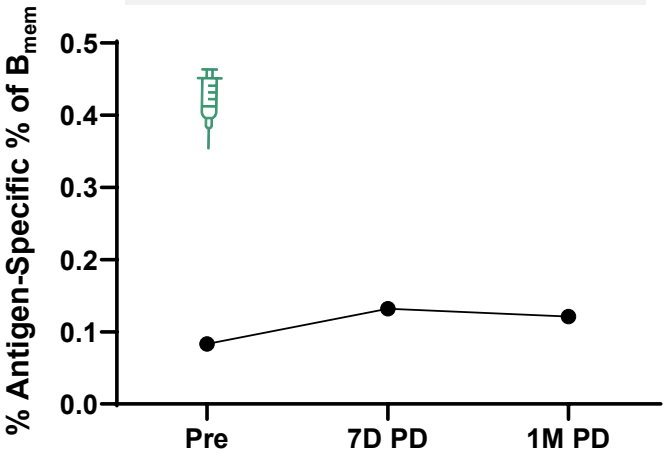


Spike WT-Specific





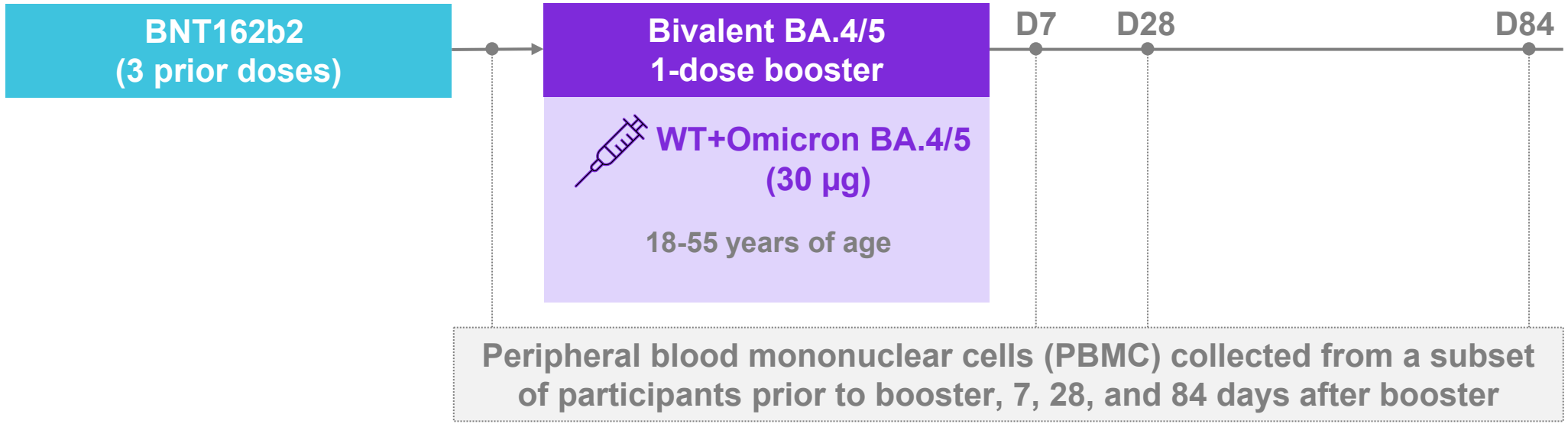
Spike BA.1-Specific



Similar trends were observed with a monovalent Omicron BA.1 booster

N=13; Memory B cells (Bmem) defined as CD3−CD19+CD20+IgD−CD38int/low.

Clinical Study Evaluated CD4 and CD8 T Cell Responses Elicited by Bivalent Omicron BA.4/5-Adapted Booster



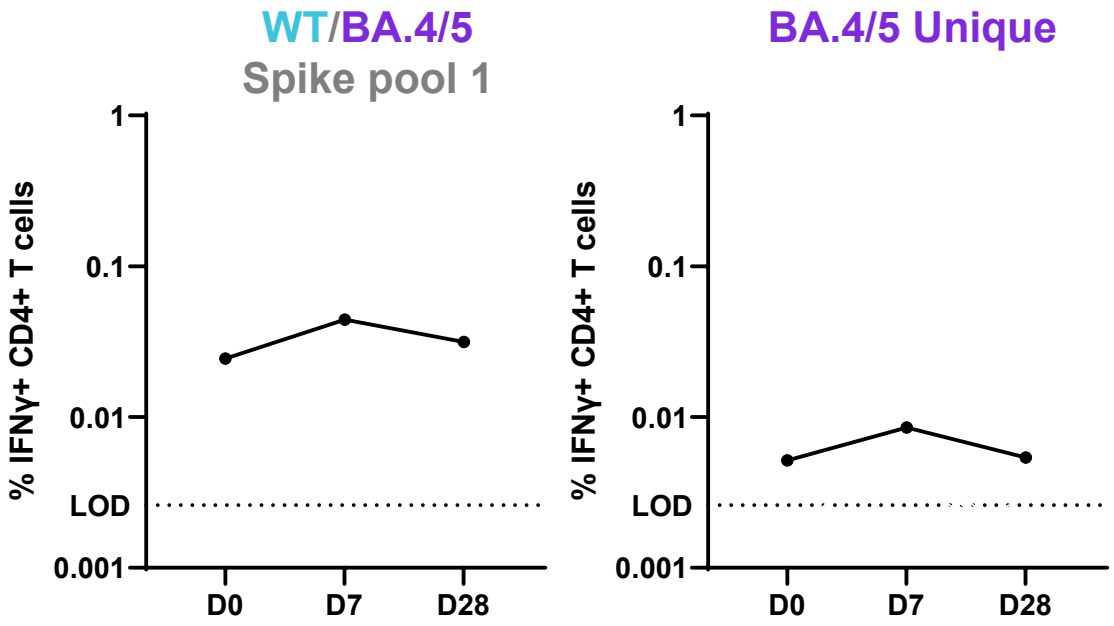
Spike peptide pools included those:

- Covering both WT and BA.4/5
- Unique to BA.4/5

Bivalent WT+BA.4/5 Vaccine Boosts CD4 and CD8 T cell Responses

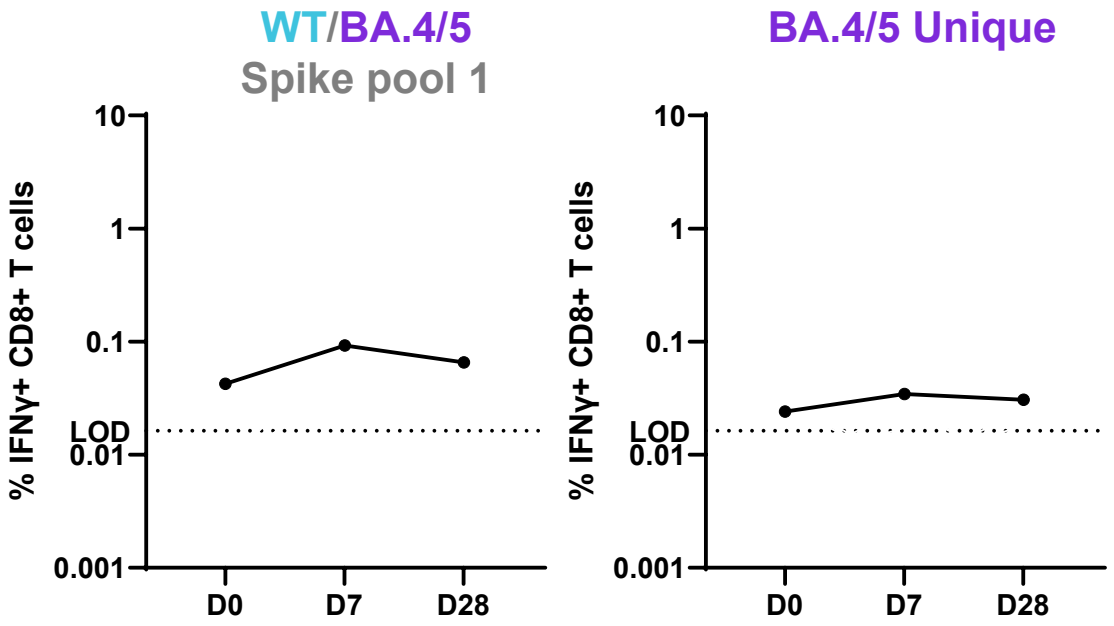
Omicron BA.4/5 Booster in BNT162b2-experienced Individuals 18-55 Years of Age

CD4 T cells



GMFR (n=20)	1.8	1.3	1.4	1.0
Pos (n=14)	1.8	1.1	1.5	1.0
Neg (n=6)	1.9	1.7	1.3	1.2

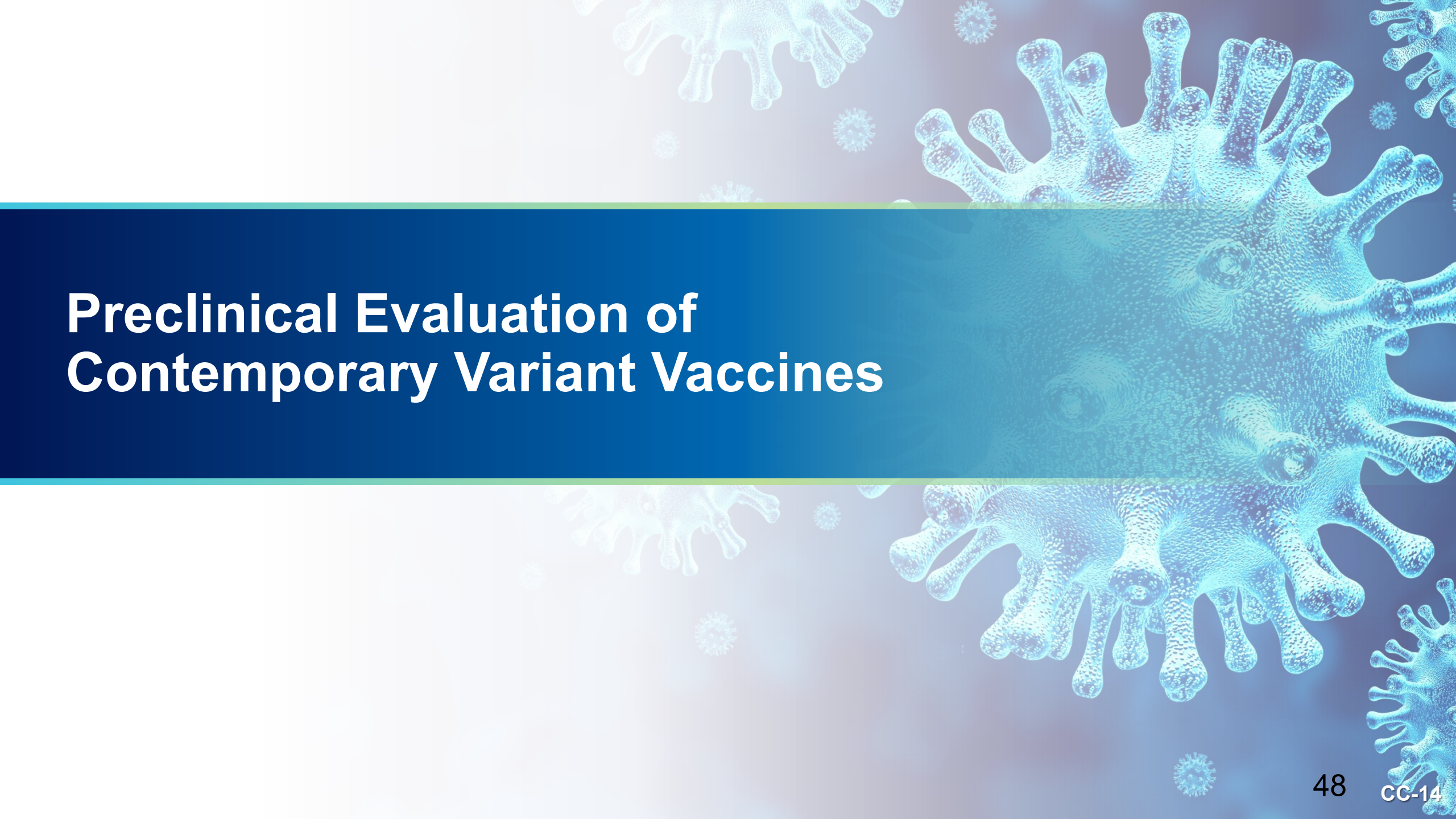
CD8 T cells



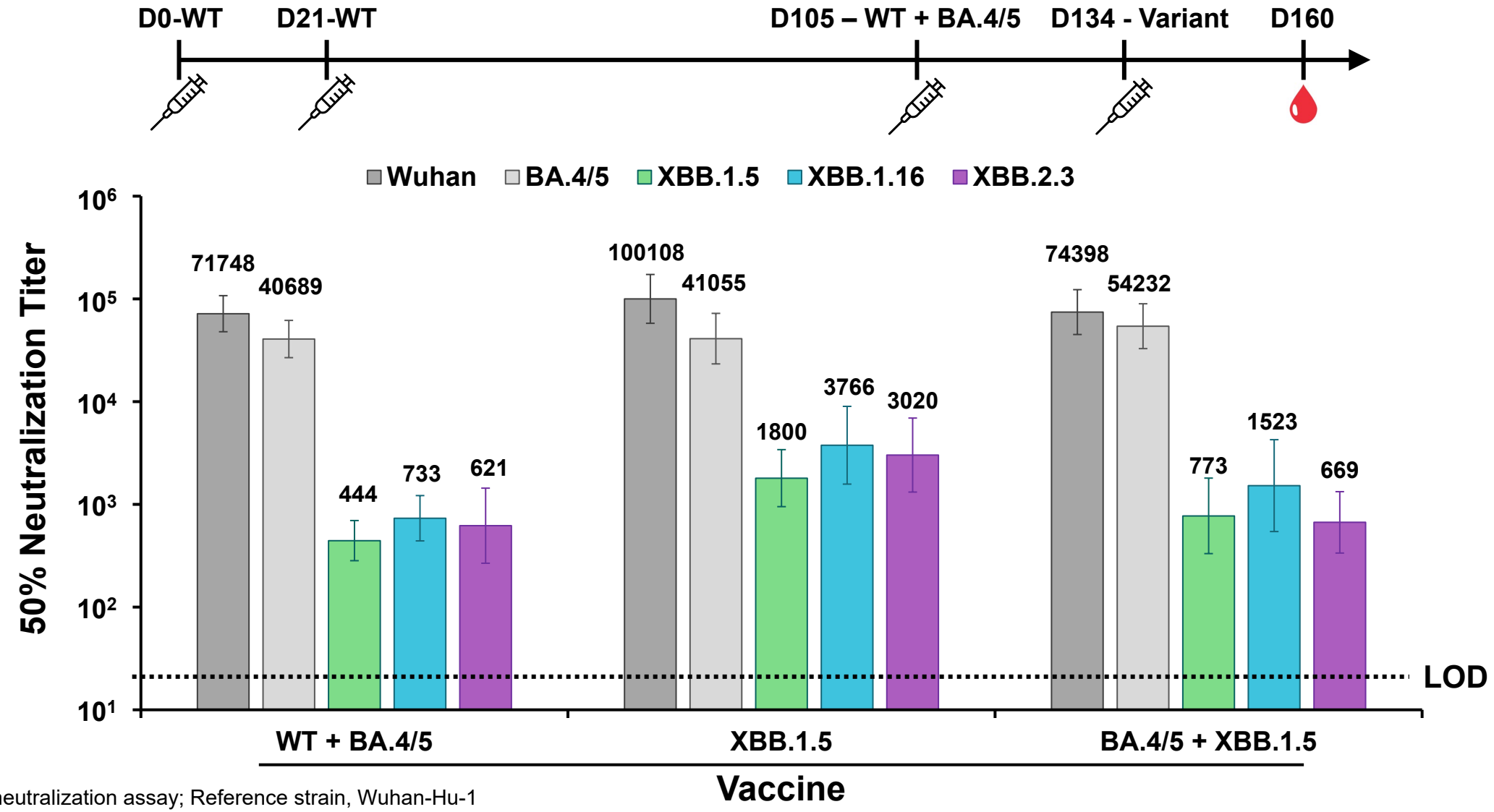
	1.9	1.4	1.4	1.2
	1.7	1.2	1.4	1.3
	2.6	1.9	1.5	1.2

WT/BA.4/5 Spike pool 1: Pool of peptides representing aa 1-643 of WT and BA.4/5
BA.4/5 Unique: Pool of peptides representing mutations unique to BA.4/5

Preclinical Evaluation of Contemporary Variant Vaccines

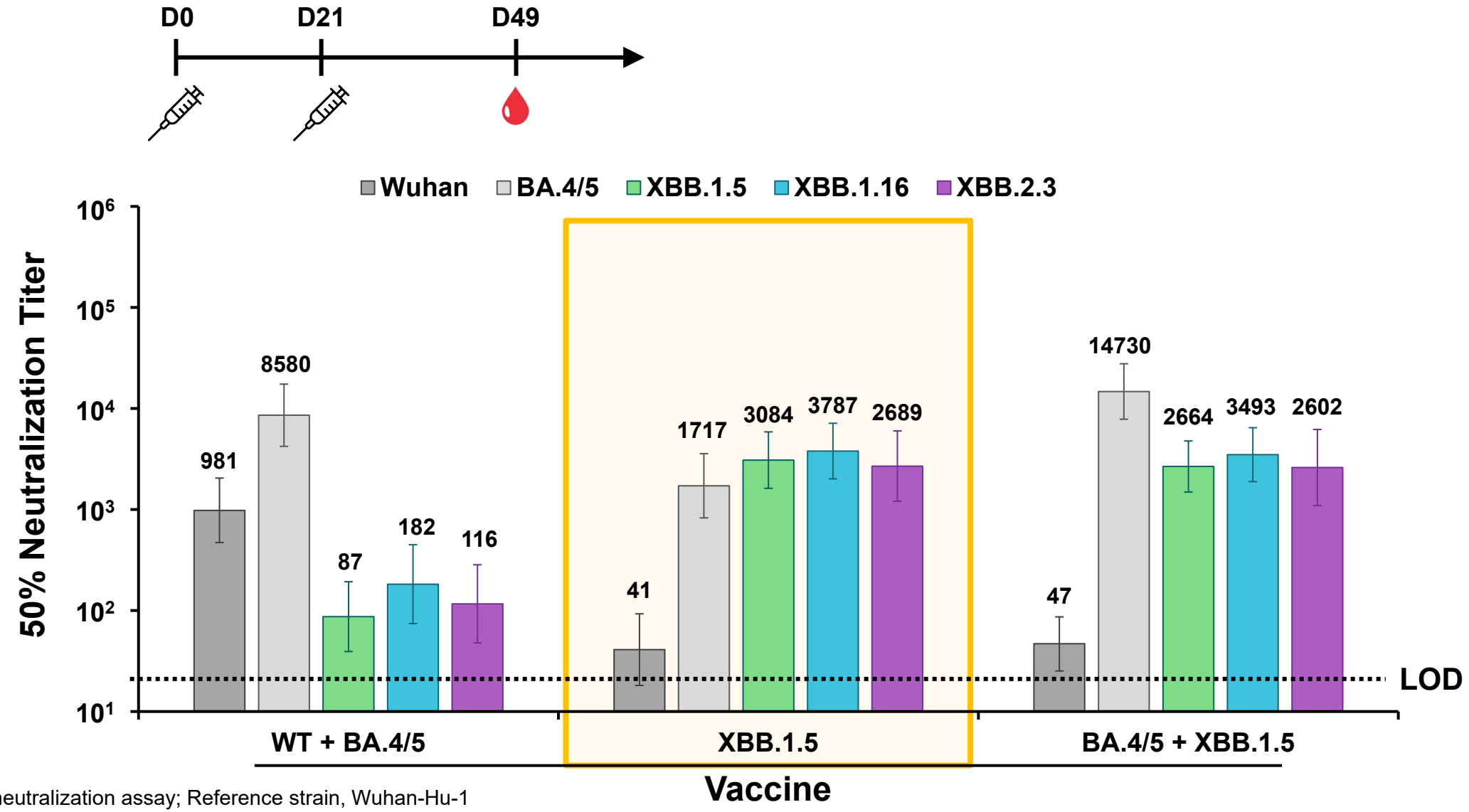


Monovalent XBB.1.5 Booster Elicits Highest XBB Sublineage Neutralization Response



Pseudovirus neutralization assay; Reference strain, Wuhan-Hu-1
LOD = Limit of detection; the lowest serum dilution of 1:20. N = 10 mice per vaccine group

Monovalent XBB.1.5 Vaccine, as a Primary Series, Elicits Highest XBB Sublineage Neutralization Response



Pseudovirus neutralization assay; Reference strain, Wuhan-Hu-1
LOD = Limit of detection; the lowest serum dilution of 1:20. N = 10 mice per vaccine group

CC-16

Supply Readiness

Readiness to Supply Updated COVID-19 Vaccine

- **Dose distribution can begin as follows, subject to regulatory approval**
  - XBB.1.5 monovalent: end July
  - XBB.1.16 monovalent: August
  - Any other formulation: October

- **Note: ~60% of flu doses are distributed by end of September**
  - Above timelines for both XBB monovalent formulations enable parallel distribution of flu and COVID-19 vaccines

- **Primary presentation will be single dose units – enabling greater access and efficiency**

Should the need arise Pfizer/BioNTech can support an off-cycle strain selection at a later date

Conclusions

Preclinical and Clinical Data Support a Monovalent XBB-adapted Vaccine for the 2023-2024 Formula

- **XBB.1.5 and XBB.1.16 are most predominant in the US**
- **Improved humoral and cell-mediated immunity with Omicron-adapted vaccines**
- **Preclinical data show XBB-adapted vaccines offer improved responses against circulating strains**
  - Higher responses with monovalent than bivalent vaccines

2023-2024 COVID-19 Vaccine Formula: Pfizer/BioNTech Clinical and Preclinical Supportive Data

Vaccines and Related Biological Products Advisory Committee

June 15, 2023

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