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Safety and Immunogenicity of a 50 µg Booster Dose of Moderna COVID-19 Vaccine

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ACIP

Oct 21, 2021

EUA for Use of Moderna COVID-19 Vaccine as a Booster

FDA authorized, Oct 20, 2021

- A single Moderna COVID-19 Vaccine booster dose (0.25 mL) may be administered intramuscularly at least 6 months after completing a primary series of the Moderna COVID-19 Vaccine to individuals:
  - 65 years of age and older
  - 18 through 64 years of age at high risk of severe COVID-19
  - 18 through 64 years of age with frequent institutional or occupational exposure to SARS-CoV-2
- A single booster dose of the Moderna COVID-19 Vaccine (0.25 mL) may be administered as a heterologous booster dose following completion of primary vaccination with another authorized or approved COVID-19 vaccine. The eligible population(s) and dosing interval for the heterologous booster dose are the same as those authorized for a booster dose of the vaccine used for primary vaccination.

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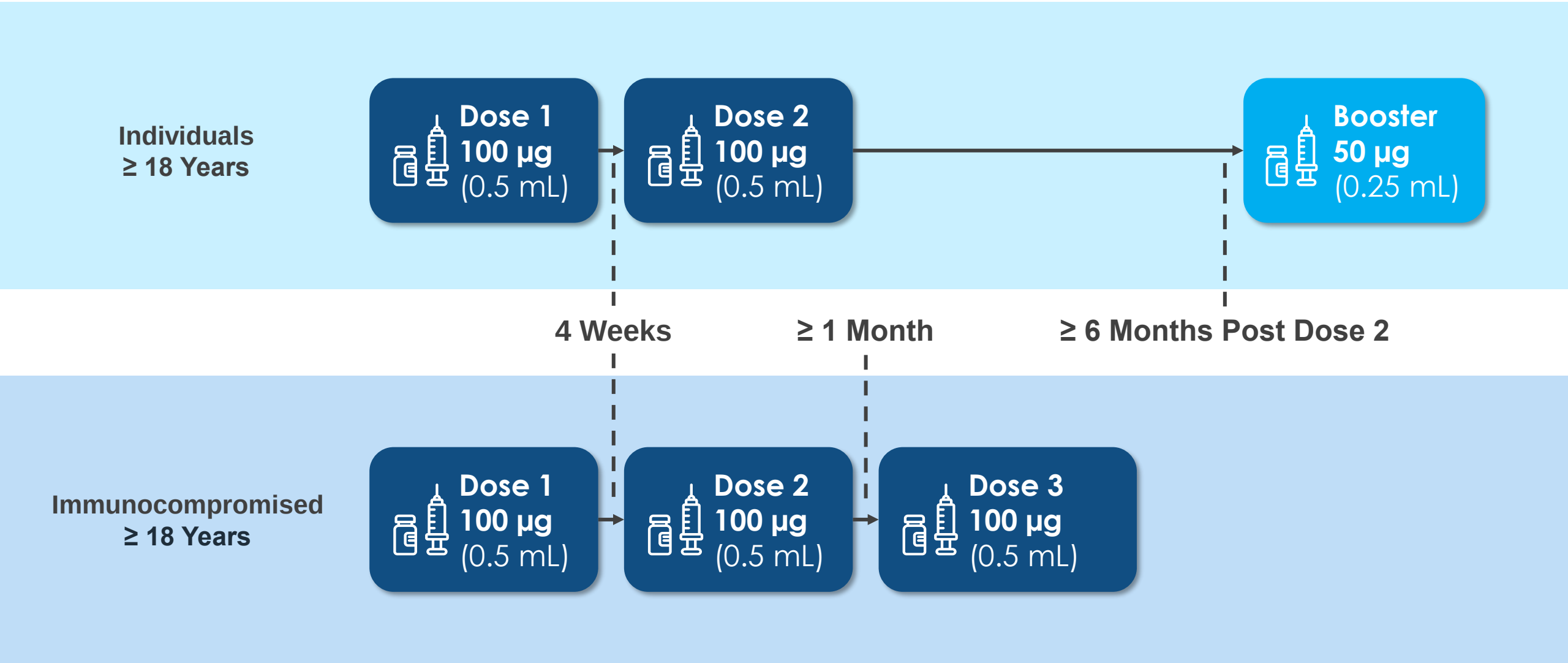
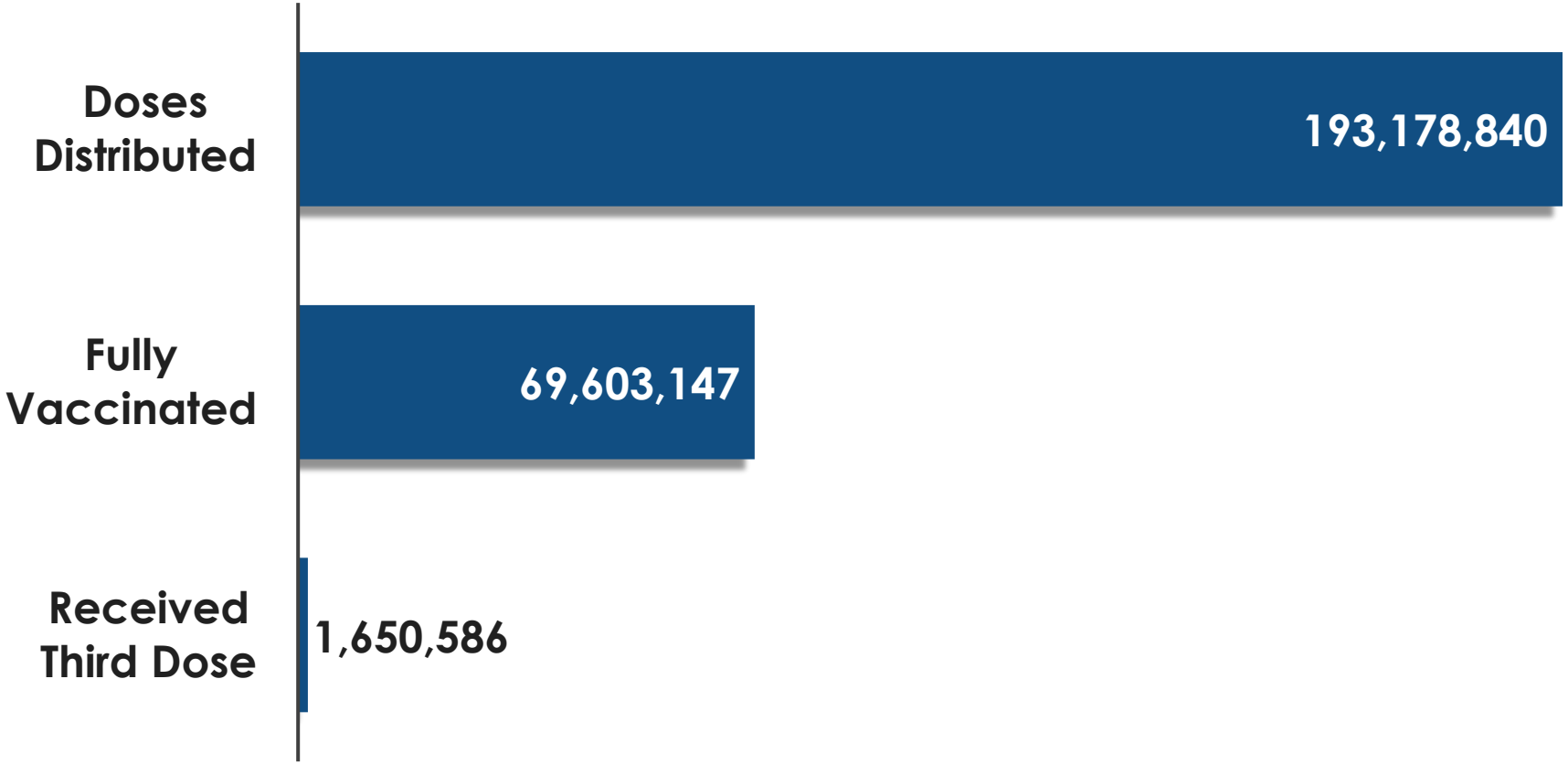
Moderna COVID-19 Vaccine
Vaccination Schedule under EUA



Use of Moderna COVID-19 Vaccine in US Since December 2020 EUA



Adapted from CDC COVID Data Tracker (as of October 20, 2021)

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Update on mRNA-1273 Efficacy through End of Blinded Phase

Phase 3 Study 301

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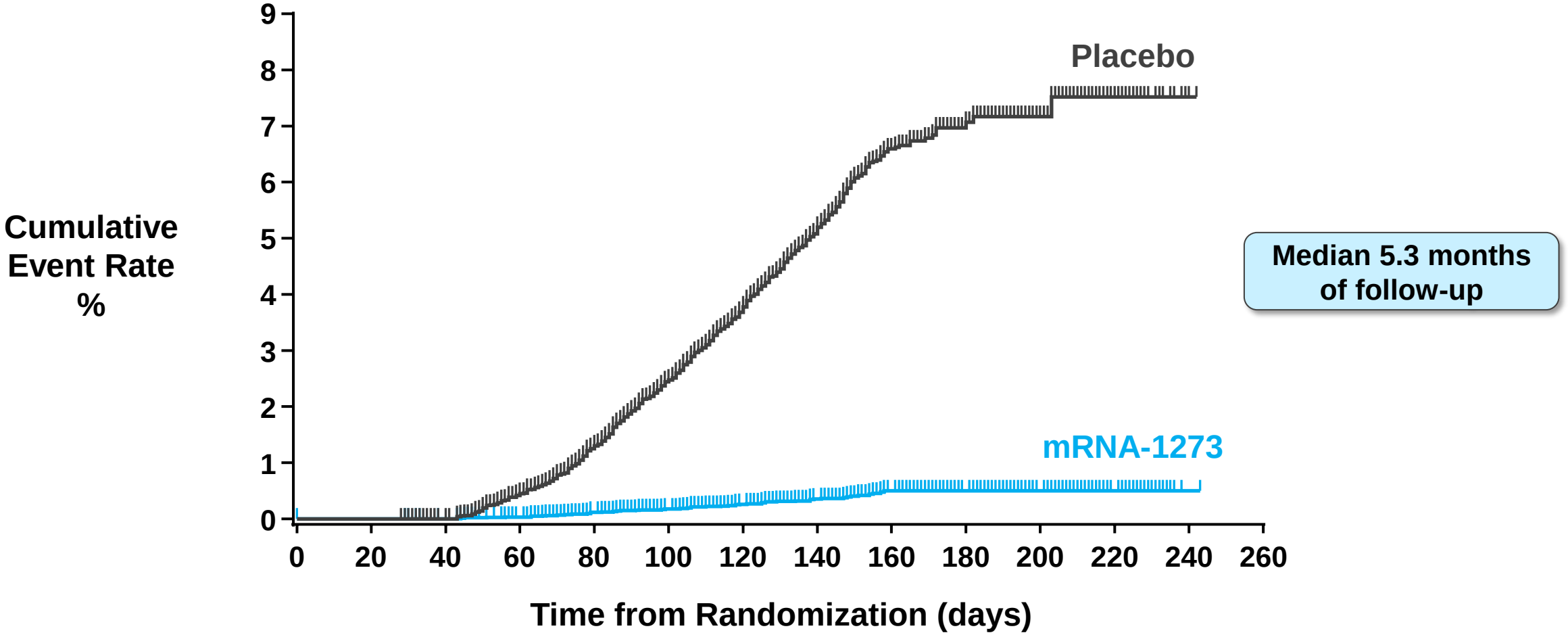
mRNA-1273 Vaccine Efficacy to Prevent COVID-19 Disease was 93.2% through 5.3 Months of Follow-up

Per Protocol Set



El Sahly, NEJM, 2021

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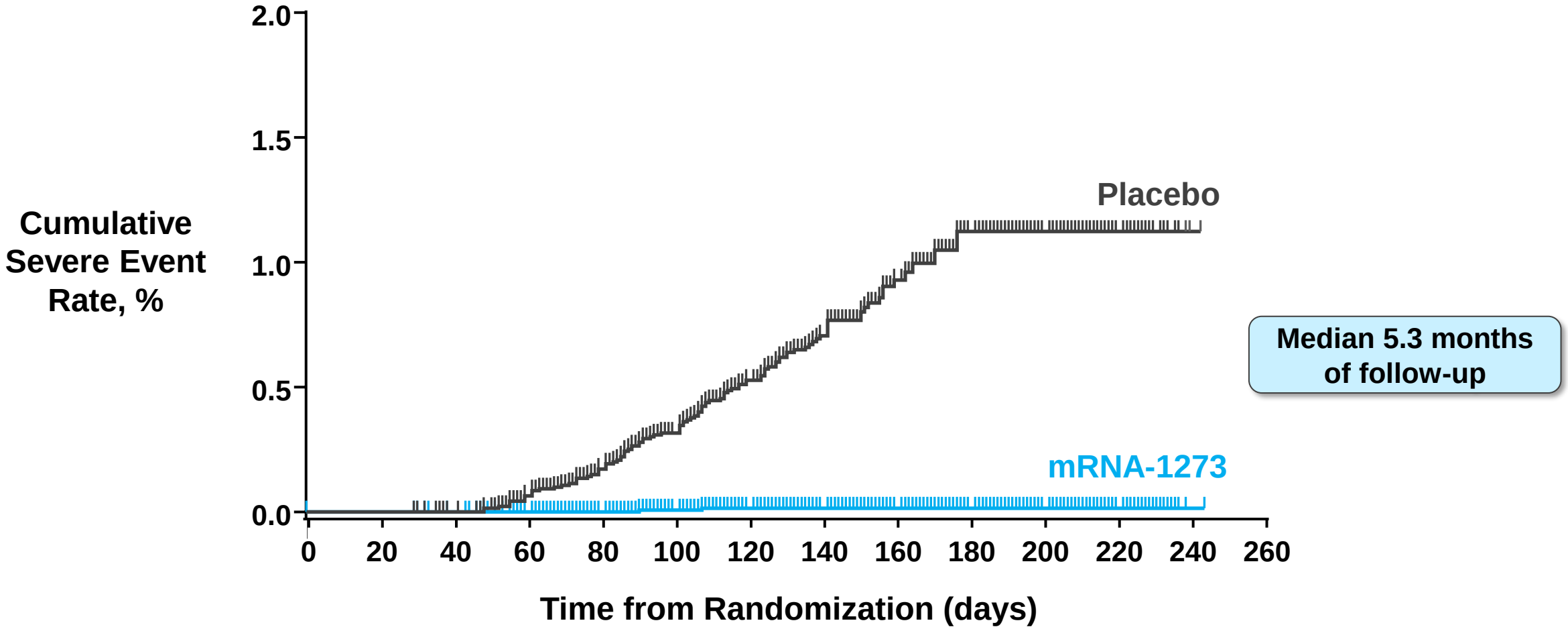
mRNA-1273 Vaccine Efficacy to Prevent Severe COVID-19 Disease was 98.2% through 5.3 Months of Follow-up

Per Protocol Set



El Sahly, NEJM, 2021

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Exploratory Analysis of Antibody Persistence and Boosting

Study 201B

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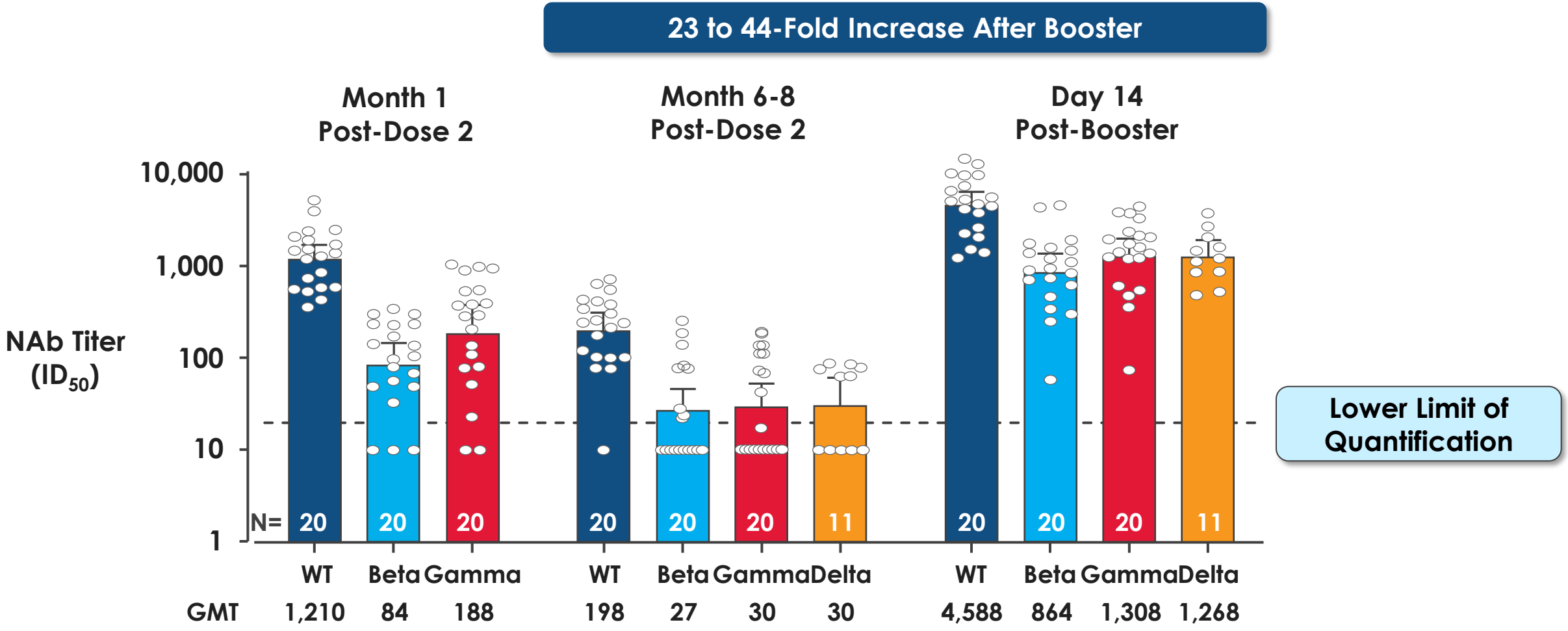
Exploratory Analysis Against Variants of Concern

Study 201B 50 µg Booster after 100 µg Primary Series (N=11-20)



WT: original strain (D614G)

Research VSV pseudoneutralization assay used; Adapted from Choi et al., Nature Medicine 2021

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COVID-19 Disease in Vaccinated Individuals from July to August, 2021

Phase 3 Study 301

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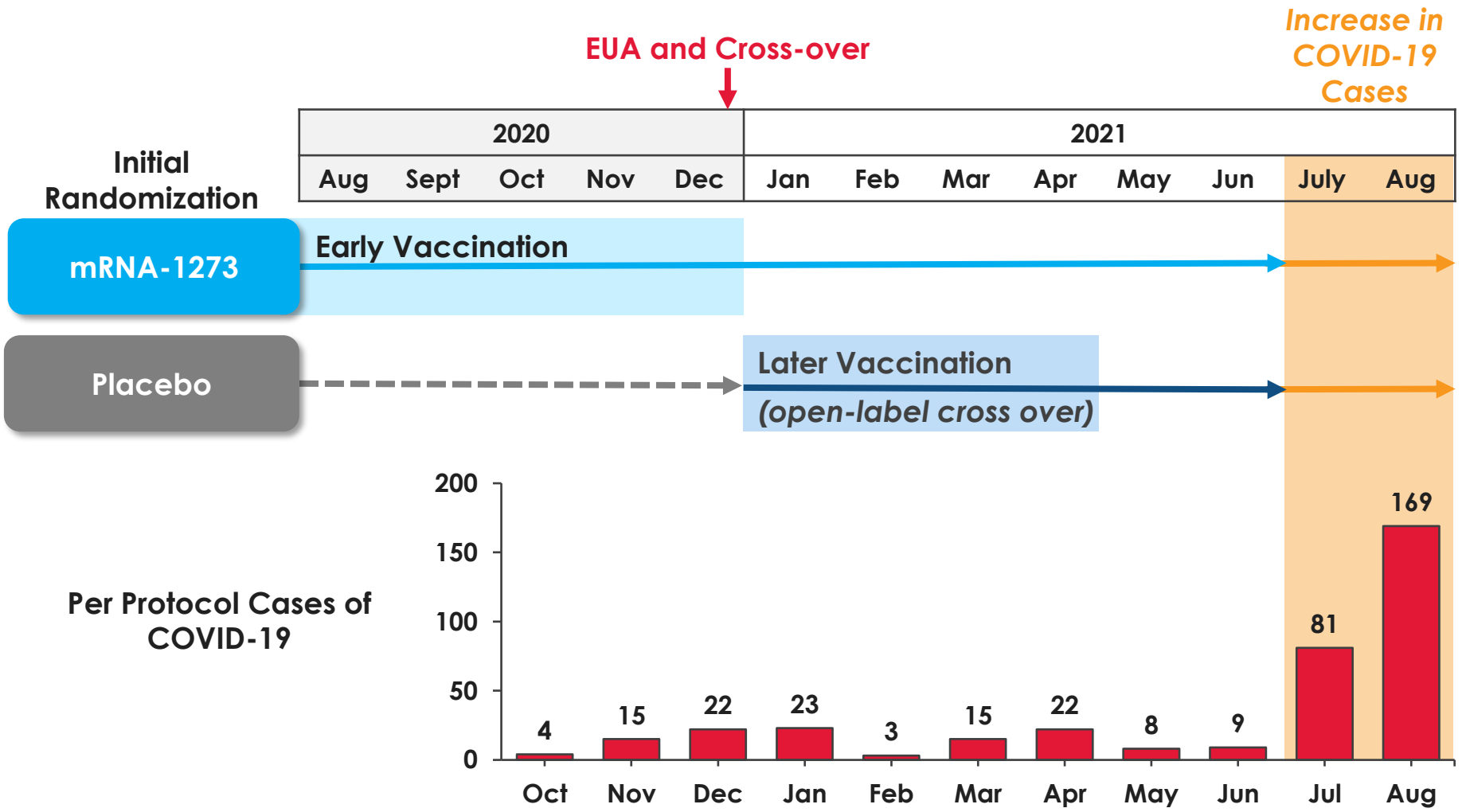
COVID-19 Cases by Month in Vaccinated Subjects

Study 301



mITT Population

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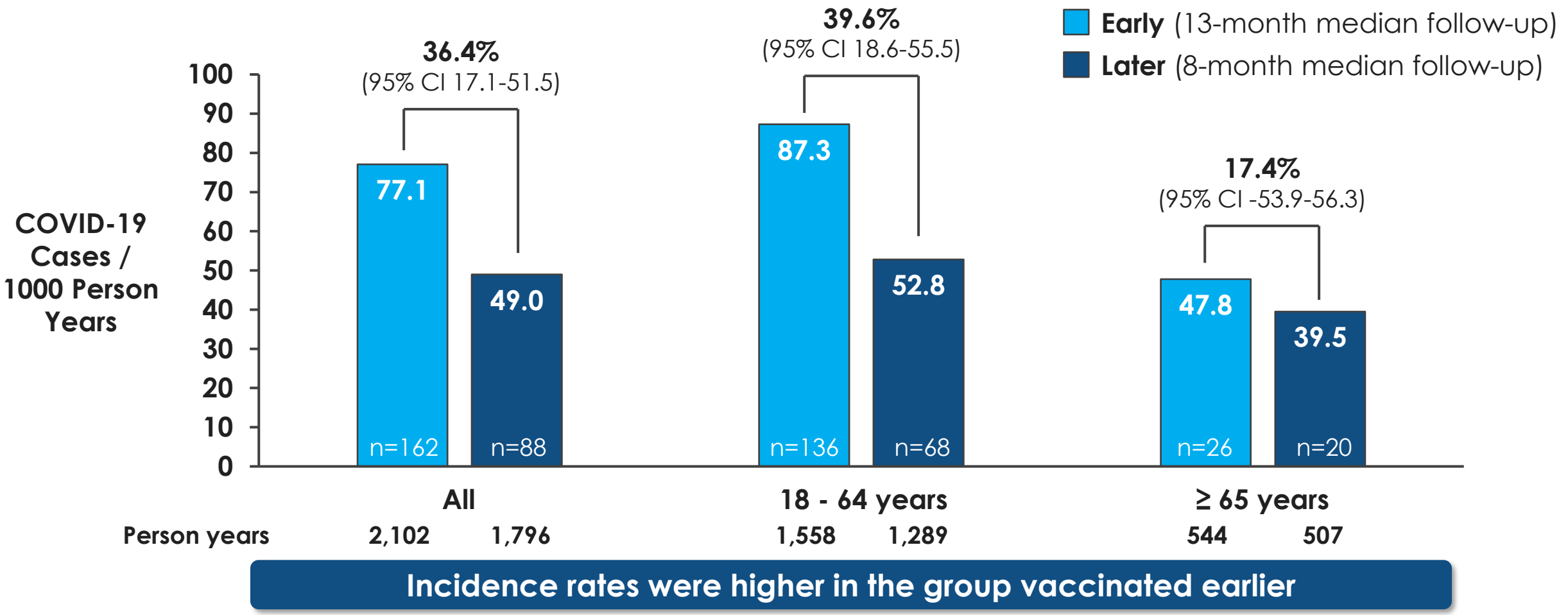
Incidence Rates of COVID-19 in Early and Later Vaccinated Groups, July – August 2021

Study 301



Median follow-up from 1st dose; Analysis of breakthrough cases observed from July 1 to August 27, 2021, mITT population
Baden et al., MedRxiv, 2021

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50 µg Booster of mRNA-1273 in Previously Vaccinated Individuals

Study 201B

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Rationale for Booster Dose Selection

- Goal was to use optimal effective dose for boosting
- Lower booster doses than those used for primary series of other vaccines shown to reactivate immune memory
- Lower booster dose increases worldwide vaccine supply of mRNA-1273

Vaccine Effectiveness of 50 µg Booster Dose Inferred by Immunobridging to Study 301

Study	N	Previous Dose of mRNA-1273 Doses 1 & 2	Booster Dose	Interval between Dose 2 & Booster Dose
201B (boost with mRNA-1273)	**146**	**50 µg**	**50 µg**	**≥ 6 months**
	149	**100 µg**	**50 µg**	
301 Immunogenicity Subset	**1,055**	**100 µg (primary series only)**	**None**	**-**

Per protocol set

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Demographic Characteristics

Study 201B Safety Set

		50 µg Booster After 100 µg Primary Series N = 171	50 µg Booster Pooled N = 344
Age	Mean (years)	52	52
	18-64	78%	76%
	≥ 65	22%	24%
Sex	Female	61%	66%
Race	White	96%	95%
	Black or African American	3%	2%
	Asian	< 1%	< 1%
	American Indian or Alaska Native	< 1%	< 1%
Ethnicity	Hispanic or Latino	6%	6%
	Not Hispanic or Latino	94%	94%

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Safety Data for 50 µg Booster After 100 µg Primary Series

Study 201B

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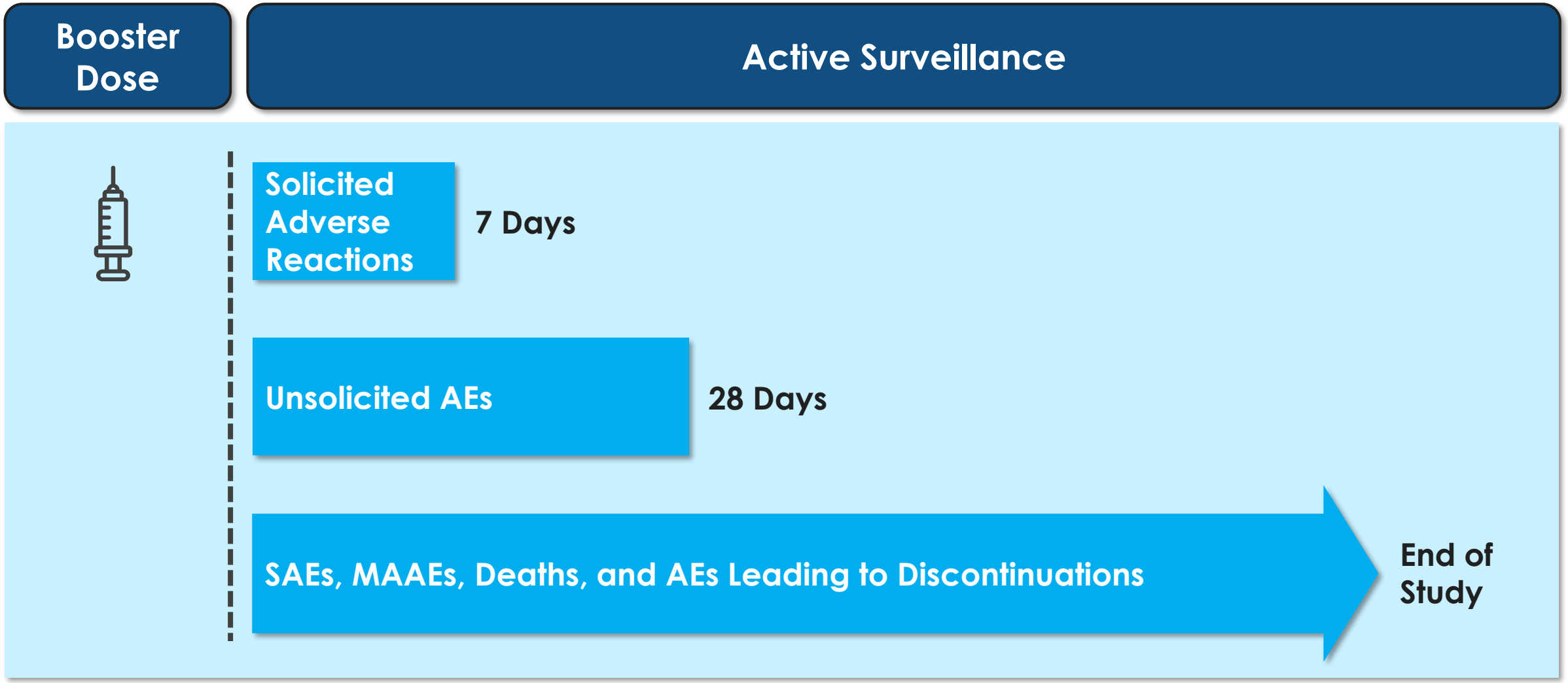
Follow-up Period for Safety Data Collection

Median 5.7 Months Safety Follow-up



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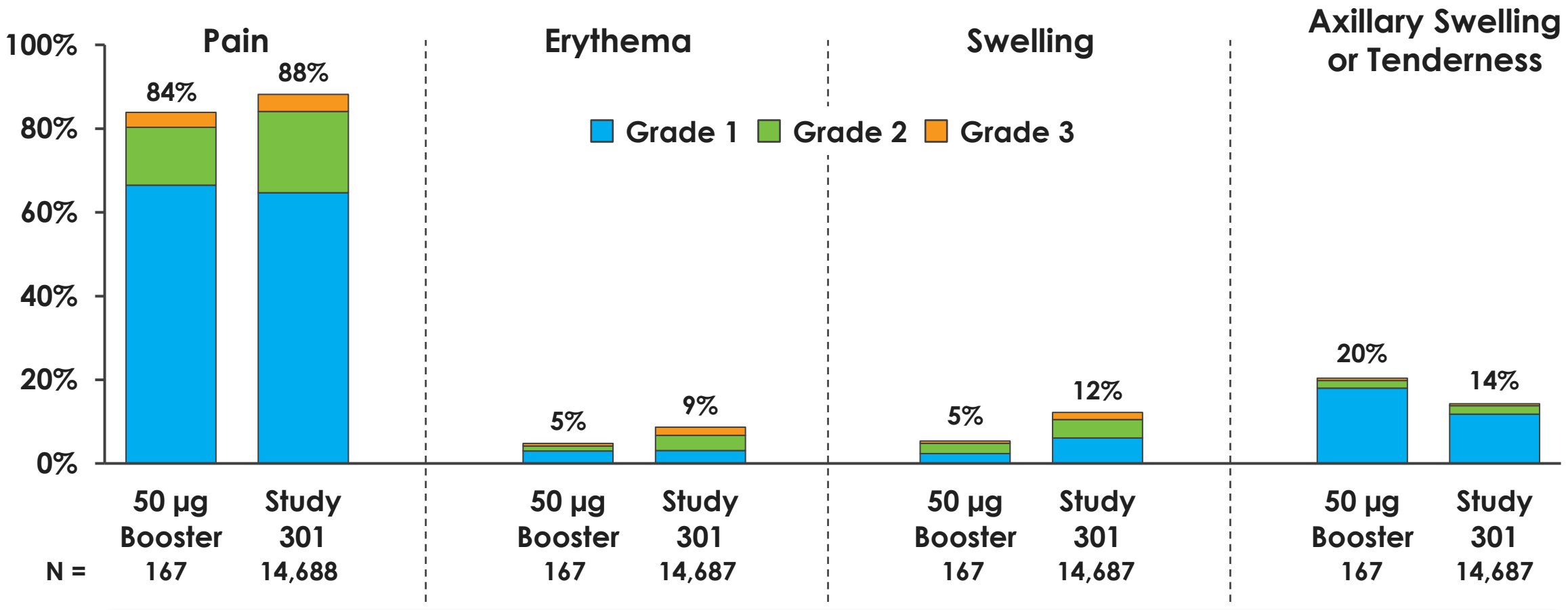
Solicited Local Adverse Reactions within 7 Days

Study 201B 50 µg Booster Dose After 100 µg Primary Series vs Study 301



Local reactions were generally similar for booster dose and Dose 2 of primary series

No Grade 4 solicited local adverse reactions were reported
Solicited safety set

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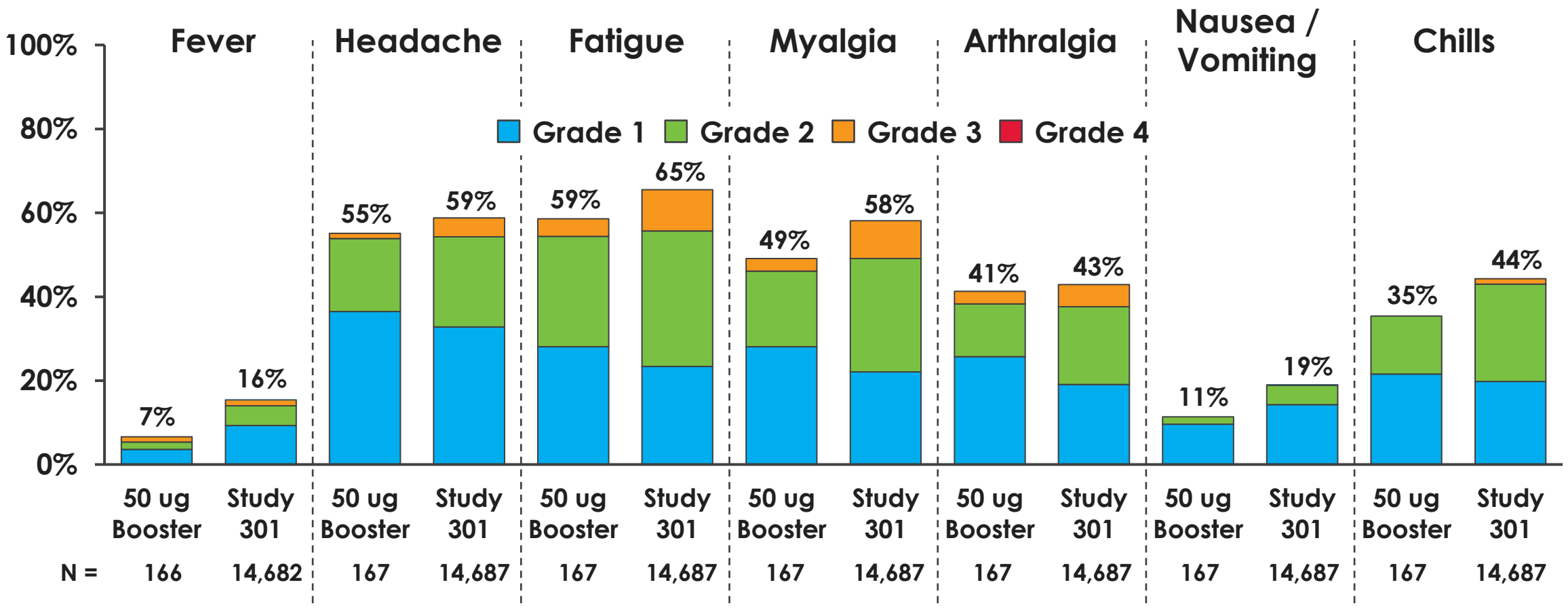
Solicited Systemic Adverse Reactions within 7 Days

Study 201B 50 µg Booster Dose After 100 µg Primary Series vs Study 301



Systemic reactions were generally similar after booster dose compared to Dose 2 of primary series

Grade 4 fever & nausea/vomiting occurred in < 0.1% of subjects in Study 301.
No Grade 4 solicited systemic adverse reactions reported in Study 201B.
Solicited safety set

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Unsolicited Adverse Events

Study 201B 50 µg Booster Dose vs Study 301

	Participants Reporting at Least One Event, n (%)		
	50 µg Booster After 100 µg Primary Series N = 171	50 µg Booster Pooled N = 344	Study 301 N = 15,184
Medically attended AEs (MAAE)	41 (24%)	78 (23%)	3,468 (23%)
Vaccine-related MAAE	2 (1%)	2 (< 1%)	213 (1%)
Serious adverse events	2 (1%)	4 (1%)	268 (2%)
Vaccine-related SAE	0	0	12 (< 0.1%)
Deaths	0	0	17 (0.1%)
Adverse event leading to study discontinuation	0	0	26 (0.2%)

No vaccine-related SAEs or deaths in Study 201B to date

As of August 16, 2021 (median 5.7 months safety follow-up)

Immunogenicity of 50 µg Booster Dose – Original Strain and Delta Variant

Study 201B

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Geometric Mean Ratio (GMR) of Neutralization Titers (Pre-specified Hypothesis)

Study 201B (Pooled) vs Study 301

Geometric Mean Titer (95% CI)		
28 days Post Booster Study 201B Pooled N = 295	**28 days Post Dose 2 Study 301** N = 1,053	**Post Booster / Post Dose 2 GMR (95% CI)**
1,768 (1,586, 1,970)	**1,033** (974, 1,095)	**1.7** (1.5, 1.9)

First co-primary endpoint of GMR non-inferiority margin of 1.5 and point estimate of ≥ 1.0 met

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Geometric Mean Ratio (GMR) of Neutralization Titers

Study 201B 50 µg Booster Dose After 100 µg Primary Series vs Study 301

Geometric Mean Titer (95% CI)		
28 days Post 50 µg Booster after 100 µg Primary Series Study 201B N = 149	**28 days Post Dose 2 Study 301** N = 1,053	**Post Booster / Post Dose 2 GMR (95% CI)**
1,802 (1,548, 2,099)	**1,027** (968, 1,089)	**1.8** (1.5, 2.1)

Co-primary endpoint of GMR non-inferiority margin of 1.5 and point estimate of ≥ 1.0 also met for 100 µg Primary Series followed by 50 µg Booster

Per protocol set
Measured as pseudovirus neutralization ID50

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Seroresponse Rates based on 3.3-Fold Definition (Prespecified Hypothesis)

Study 201B (Pooled) vs Study 301

	Study 201B 50 µg Booster Pooled N = 294	Study 301 100 µg Primary Series N = 1,050
Baseline Geometric Mean Titer (GMT)	126	10
GMT 28 days post dose	1,893	1,081
Participants achieving seroresponse, n (%)	275 (94%)	1,038 (99%)
95% CI	90.1, 96.1	98.0, 99.4
Difference in seroresponse rate (SRR)	-5.3	
95% CI	-8.8, -2.9	

Co-primary endpoint of SRR met (lower bound of 95% CI ≥ -10%)

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Seroresponse Rates Based on 4-Fold Rise from Pre-Booster Titers

Study 201B 50 µg Booster after 100 µg Primary Series vs Study 301

	50 µg Booster After 100 µg Primary Series N = 149	Study 301 100 µg Primary Series N = 1,050
Baseline Geometric Mean Titer (GMT)	150	10
GMT 28 days post dose	1,952	1,081
Participants achieving seroresponse, n (%)	131 (88%)	1,033 (98%)
95% CI	81.6, 92.7	97.4, 99.1
Difference in seroresponse rate (SRR)	-10.5	
95% CI	-16.7, -6.1	

SRR success criteria not met (lower bound of 95% CI ≥ -10%)

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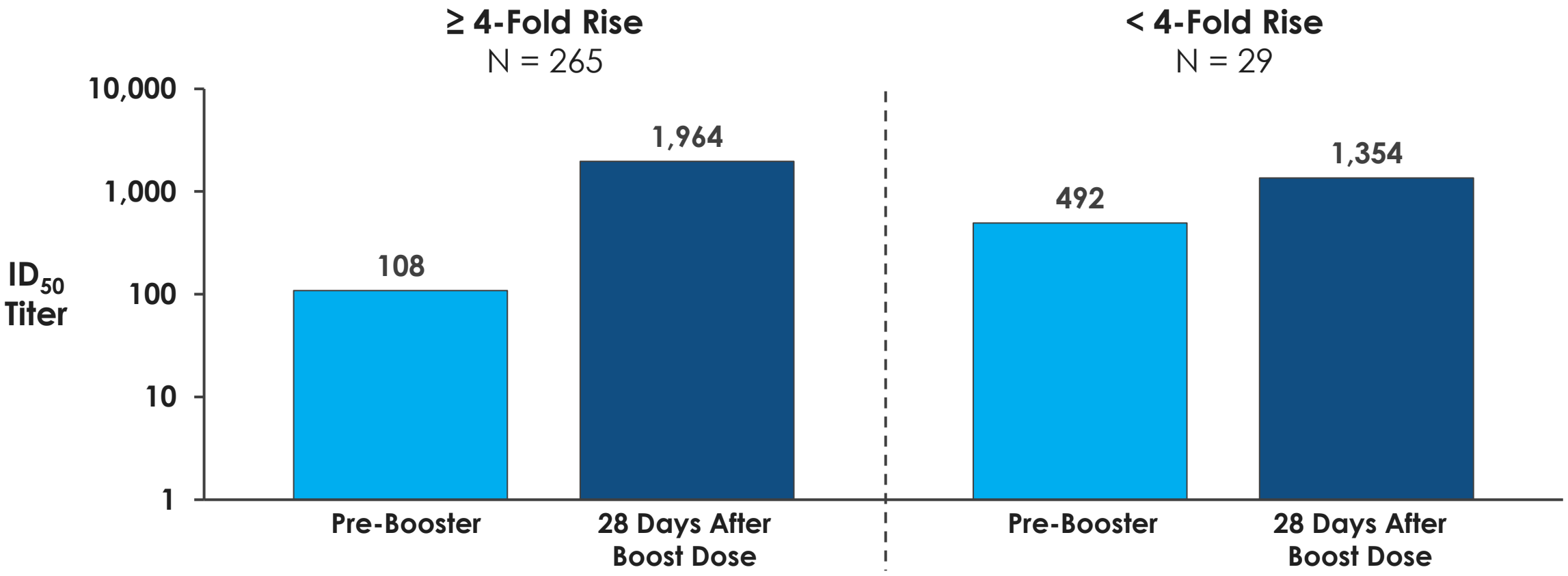
Neutralizing Antibody Titer Comparison for Subjects Who Had ≥ 4-Fold Rise vs < 4-Fold Rise to Original Strain D614G after Booster Dose

Study 201B (Pooled)



Subjects who did not meet 4-fold rise had 4 times higher pre-booster titers compared to those who did meet 4-fold rise

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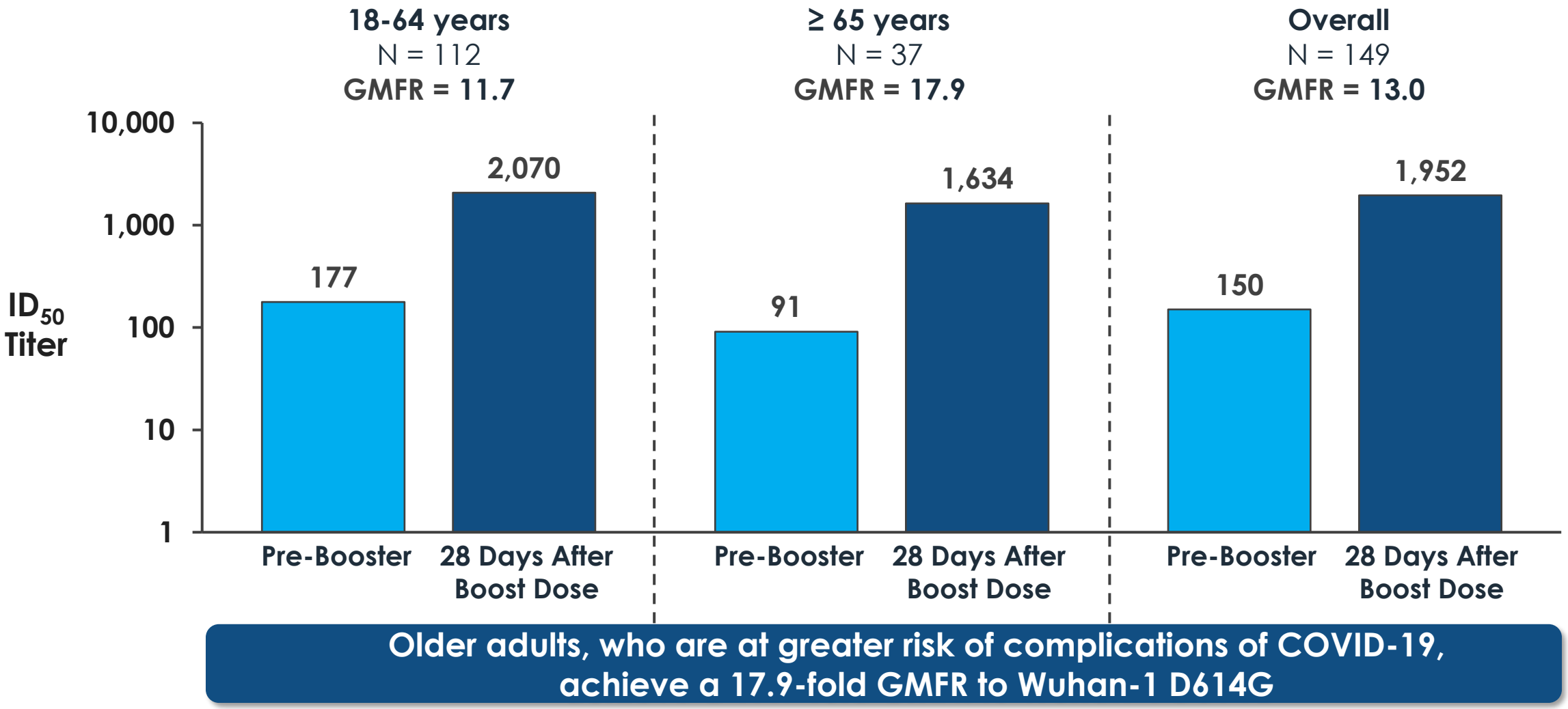
Geometric Mean Fold Rise of Neutralization Titers Against Original Strain *D614G* by Age and Overall

Study 201B 50 µg Booster after 100 µg Primary Series



Older adults, who are at greater risk of complications of COVID-19, achieve a 17.9-fold GMFR to Wuhan-1 D614G

Per protocol set
GMFR = Geometric Mean Fold Rise

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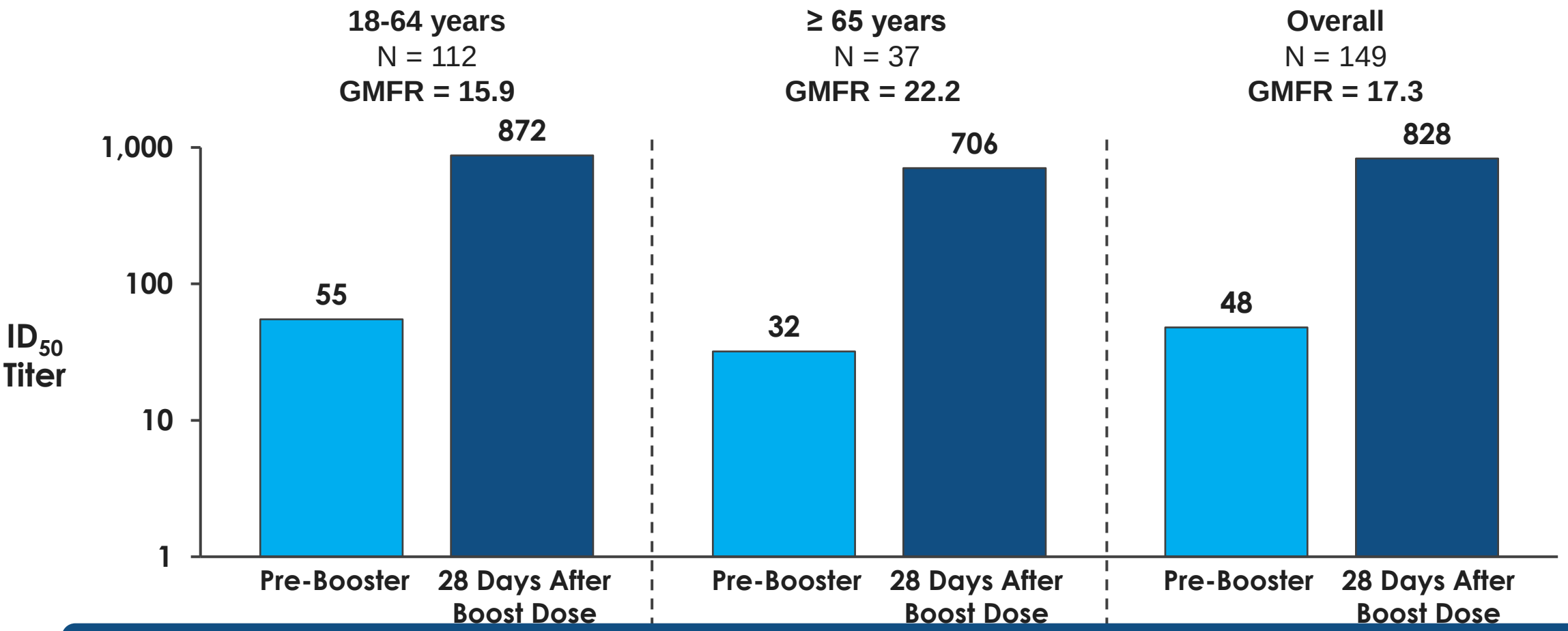
Geometric Mean Fold Rise of Neutralization Titers Against *the Delta Variant* by Age and Overall

Study 201B 50 µg Booster after 100 µg Primary Series



15.9 to 22.2-fold increase in post-boost titers against Delta was achieved in both age groups

GMFR = Geometric Mean Fold Rise

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Summary

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Safety Summary - 50 µg Booster Dose

- Rates of adverse reactions (ARs) with 50 µg booster dose comparable to those observed after Dose 2 of primary series
  - Pain at injection site most common solicited local AR in both groups
  - Headache, fatigue and myalgia most common systemic ARs in both groups
  - Majority of ARs were mild-to-moderate in severity
  - Axillary swelling or tenderness was the only AR more frequently reported after booster dose as compared to dose 2 in Study 301

- No vaccine-related SAEs or deaths in Study 201B

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Immunogenicity Summary - 50 µg Booster Dose

- Pre-specified co-primary hypotheses (GMR & SRR difference) were met on pooled dataset
- 50 µg booster dose following 100 µg primary series results in
  - Higher antibody responses to original virus (D614G) than post- dose 2 in Study 301 (GMR = 1.8)
  - 13-fold rise from pre-booster titers for original virus
  - 17-fold rise from pre-booster titers for Delta variant
- Consistently high antibody titers in both age groups (18-64 and ≥ 65 year olds)

GMR = geometric mean ratio
SRR = seroresponse rate

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THANK YOU!

- NIH/COV-PN
- All investigators at many study sites
- Study site personnel
- BARDA
- Montefiori laboratory at Duke University
- **Most importantly, the many individuals who participated in these trials**

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