RSV Vaccine (mRESVIA, mRNA-1345) Concomitant Administration Overview

Advisory Committee on Immunization Practices

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Cumulative Burden of Seasonal Respiratory Viruses in US Older Adults

	COVID-19	Influenza	RSV
Cumulative US Hospitalization Rate (≥65 yr, rate/100,000, 9/28/2024)[1]	811	227	106
US Vaccine Coverage 2023-24[2-4] (COVID-19 & Flu ≥65 yrs, RSV ≥60 yrs)	39%	70%	23%

Concomitant administration of vaccines is an effective method to increase vaccine coverage.
MMWR: Coadministration of RSV vaccines with other adult vaccines during the same visit is acceptable[5-8]

1. CDC RESP-NET, MMWR week 39, week ending 9/28/2024, https://www.cdc.gov/resp-net/dashboard/index.html accessed 10/18/2024 ; 2. CDC COVIDVaxView https://www.cdc.gov/covidvaxview/ ; 3. CDC FluVaxView https://www.cdc.gov/covidvaxview/ ; 4. CDC RSVVaxView https://www.cdc.gov/rsvvaxview/ 5. Bonanni et al Human Vaccines Immuno 2023; 6. NVAC Pediatrics. 2003;. 7. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html#ref-13; 8. Britton et al. MMWR 2024 https://www.cdc.gov/mmwr/volumes/73/wr/mm7332e1.htm

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mRNA 1345 Clinical Development

Efficacy, Immunogenicity, Safety, and Correlate of Protection

Adults ≥60 years
Study 301

Concomitant Administration with Standard Dose Influenza

Adults ≥50 years
Study 302 - Part A

Concomitant Administration with COVID-19

Adults ≥50 years
Study 302 - Part B

Concomitant Administration with High Dose Influenza

Adults ≥65 years
Study 304

NCT05127434, NCT05330975, NCT06060457

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Summary of Today's Presentation

Study 302 Parts A & B – Supports coadministration of mRNA-1345 with standard dose influenza and COVID-19 vaccines (previously presented)[1]

- Well tolerated with no safety concerns
- Robust immunogenicity observed for all influenza strains, COVID-19, and RSV

Study 304 – Data for coadministration of mRNA-1345 with high-dose influenza vaccine

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- RSV titers lower with coadministration; data from correlate of protection model demonstrate that clinical efficacy against RSV disease, including severe disease, is likely maintained

Overall, the benefit: risk of coadministration of mRNA-1345 with standard and high-dose influenza vaccines, and COVID-19 vaccine is positive

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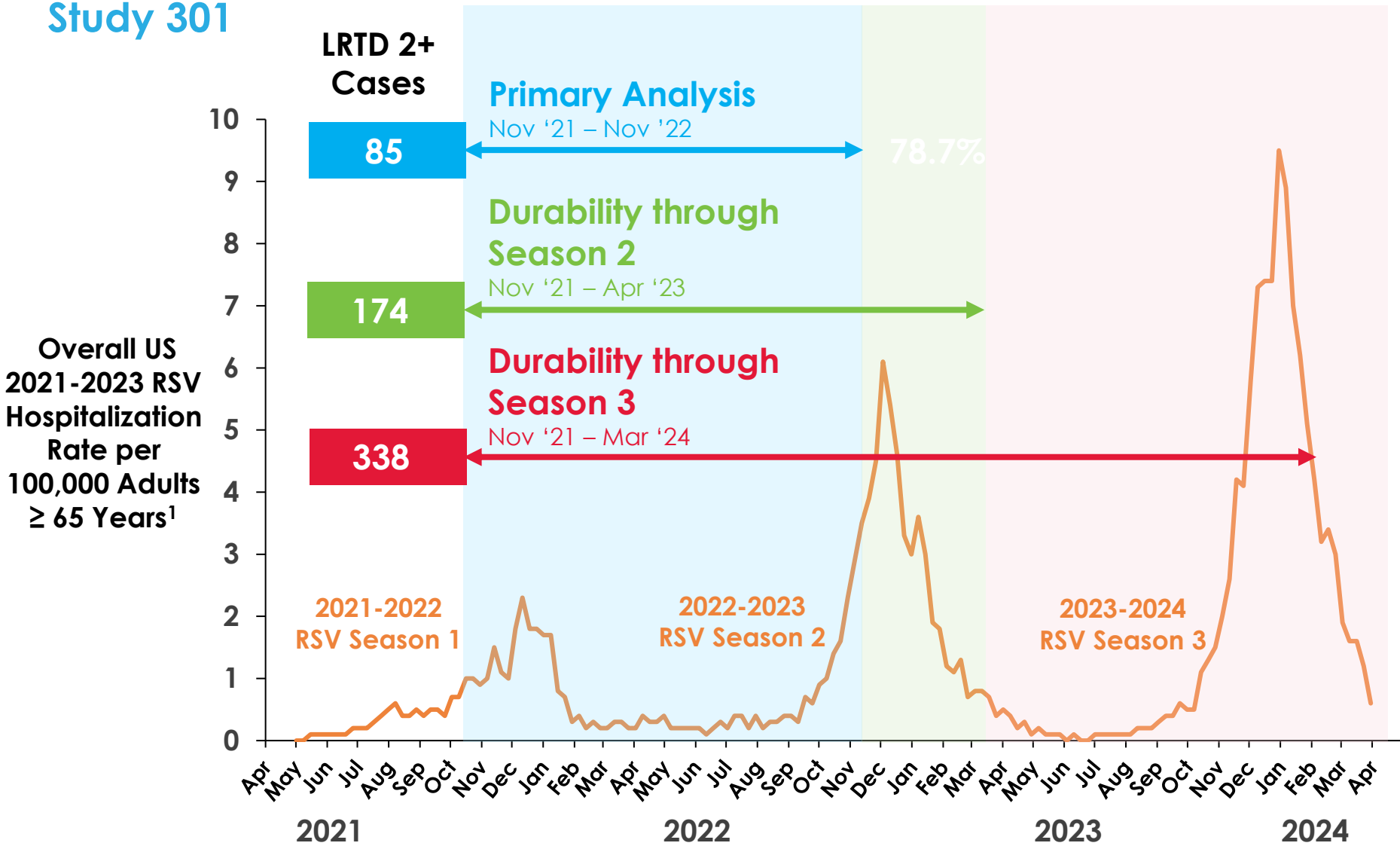
RSV Case Accrual and Efficacy Analyses through 3 Seasons in the Phase 2/3 Pivotal Trial

Study 301



Efficacy[2]

LRTD 2+	Severe RSV (shortness of breath)
78.7% (62.8%, 87.9%)	86.7% (41.9%, 97.0%)
62.5% (47.7%, 73.1%)	74.6% (50.7%, 86.9%)
50.3% (37.5%, 60.7%)	56.7% 33.1%, 72.6%)

1. CDC. Respiratory Syncytial Virus Hospitalization Surveillance Network (RSV-NET). https://www.cdc.gov/respiratory-viruses/data-research/dashboard/most-impacted-hospitalizations.html 2. Based on final FDA Package Insert

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RSV Correlate of Protection Model

Preplanned case-cohort design

INPUT from Phase 3 Pivotal Efficacy Trial
(Study 301)

- **1597 mRNA-1345 Recipients**
- **533 Placebo Recipients**
- **271 RSV ARD Cases[1]**

OUTPUT

Predicted Efficacy

- Coadministration efficacy
- Revaccination efficacy

- Day 1 and Day 29 sera collected from all study participants
- Evaluated for RSV-A and B neutralizing titers, and Pre-F binding titers
- Objective to determine the relationship between immunogenicity and efficacy to identify correlates of protection

1. Includes 174 LRTD2+ and 70 LRTD3+ RSV cases; Ma, C et al, RSVVW, 2024

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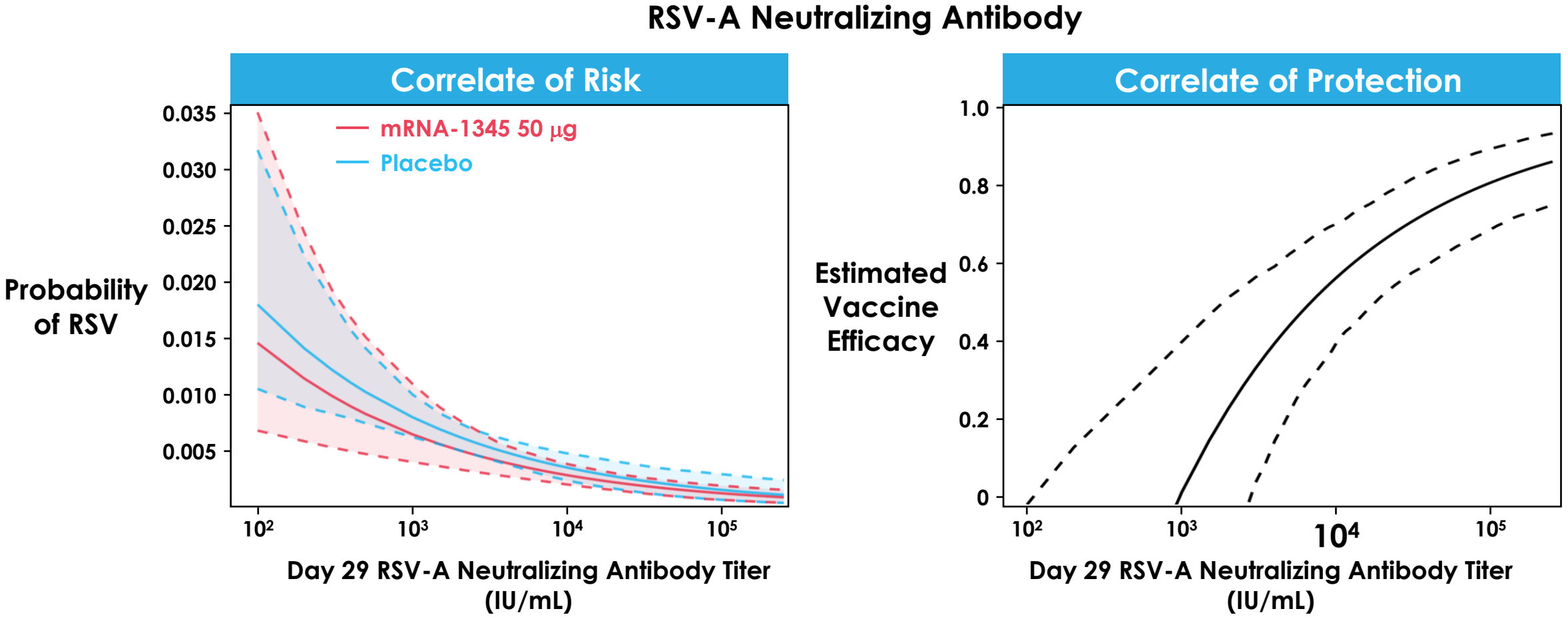
Antibodies are a Correlate of Risk and Correlate of Protection for RSV

Study 301 – LRTD2+ RSV Efficacy



The panels demonstrate the Correlate of Risk (A) and Correlate of Protection (B) analysis for the RSV-LRTD 2+ endpoint by Day 29 RSV-A neutralizing antibody.

A. The red and blue solid curves demonstrate the point estimate of the predictive risk for vaccine and placebo recipients at each assigned antibody titer. The red and blue dashed curves along with the shaded area represent the bootstrap point-wise 95% confidence interval (CI).

B. The solid black curve shows the point estimate of controlled vaccine efficacy at each assigned antibody titer and the dashed curves demonstrate the bootstrap point-wise 95% CI.

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Concomitant Administration of mRNA-1345 with High-Dose Influenza Vaccine

Study 304

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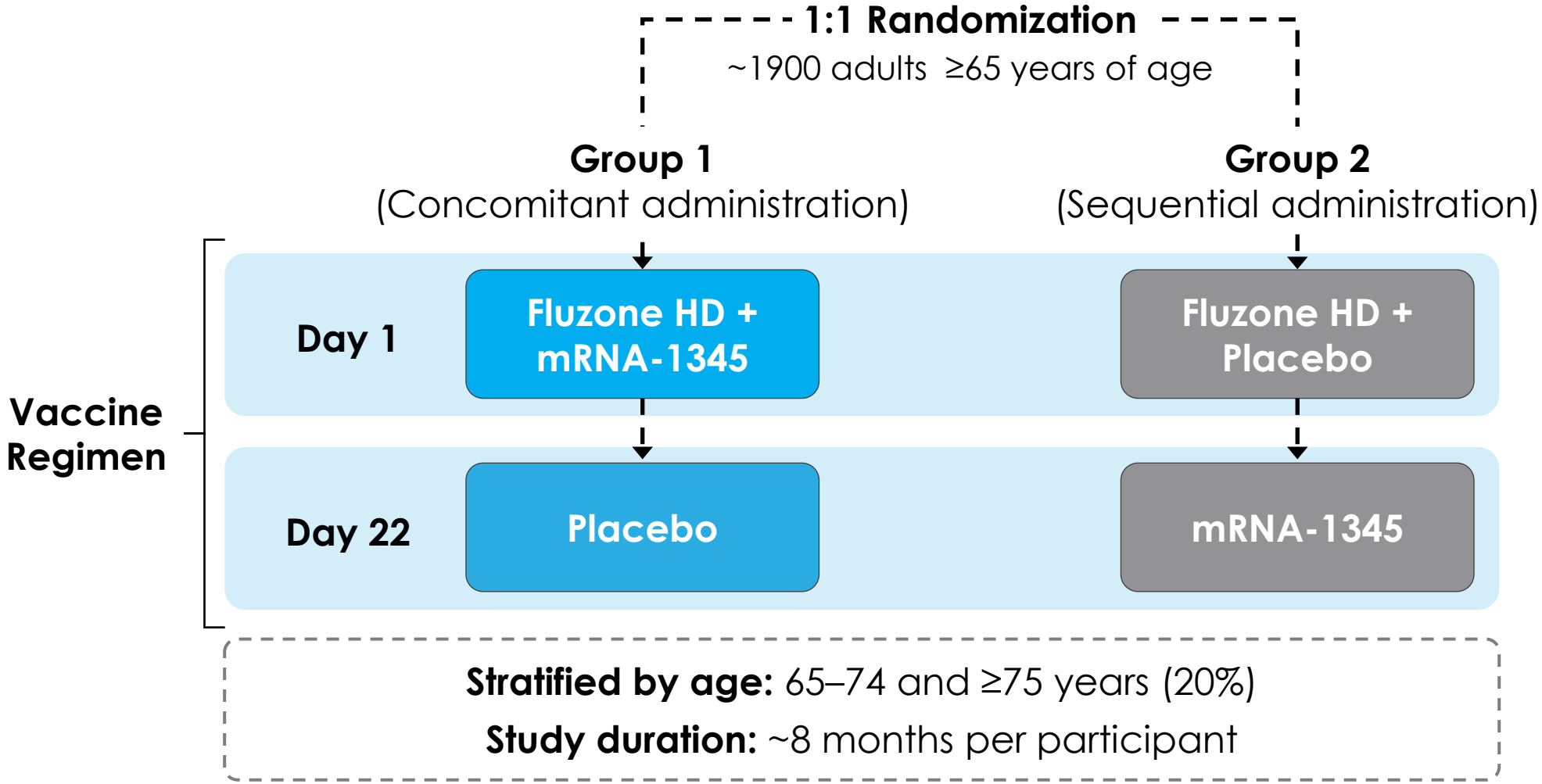
Study Design – Concomitant Administration of mRNA-1345 & Fluzone HD

United States

Study 304 - Phase 3, Randomized, Observer-Blind Trial



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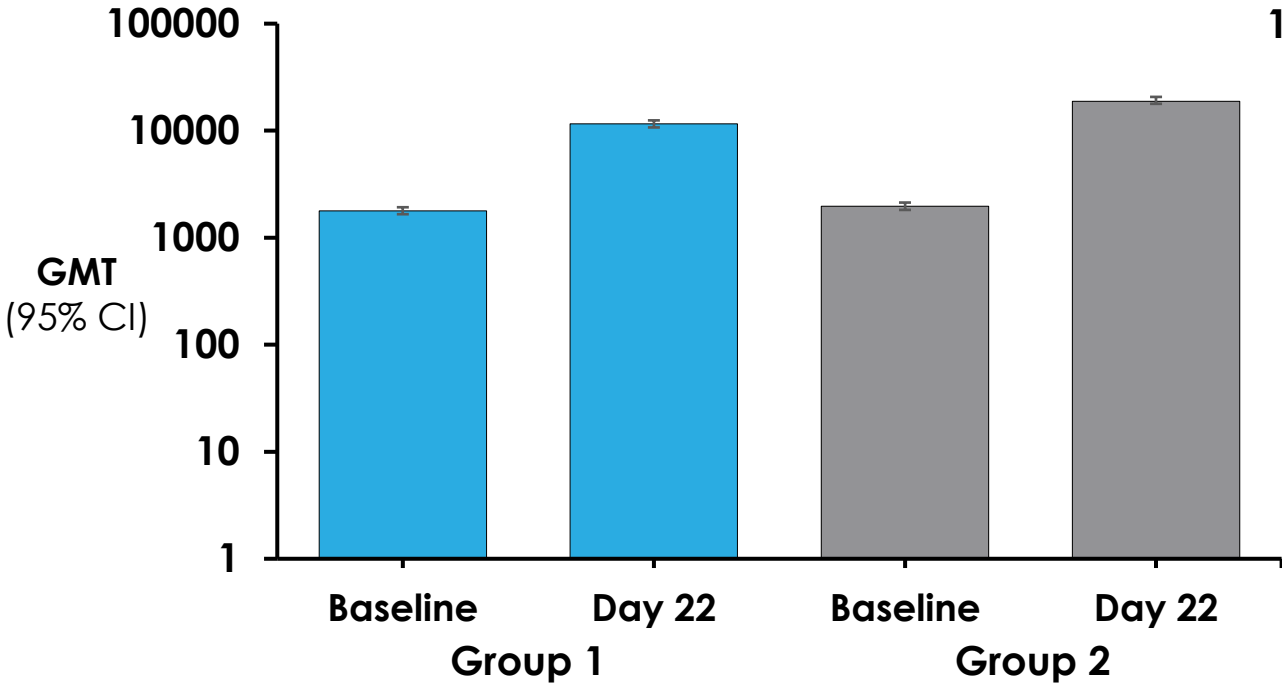
Concomitant Administration Results in Robust RSV and Influenza Responses Across All Adults ≥65 Years

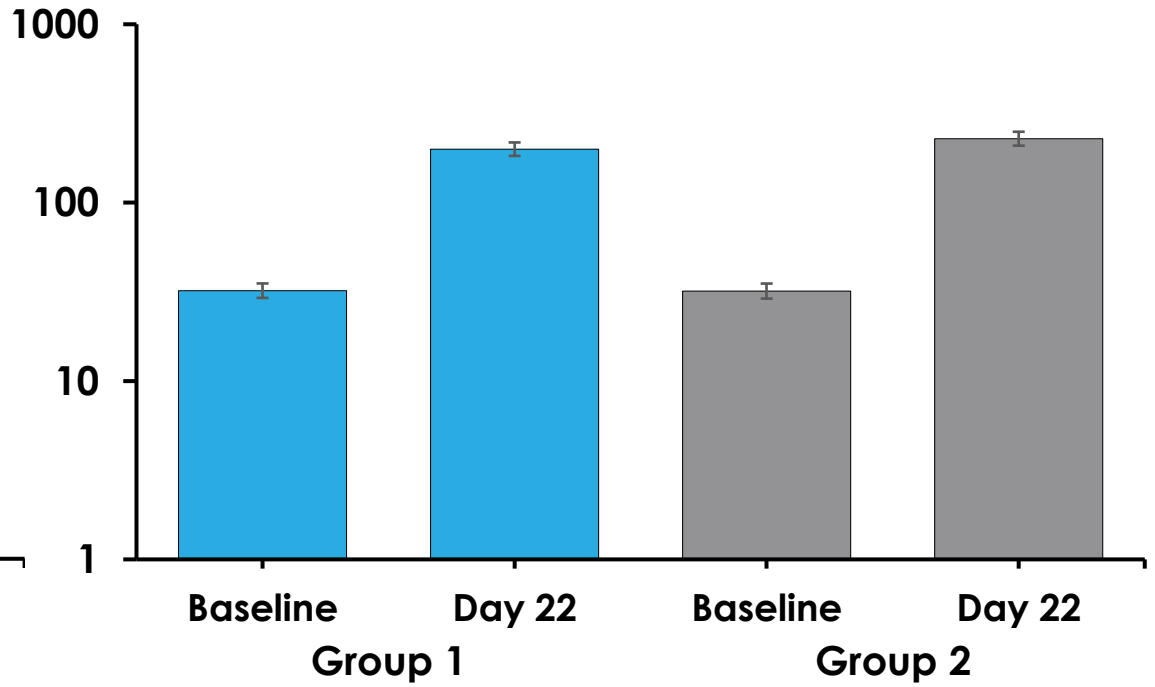
Study 304

Group 1	Group 2
D1: Flu HD + mRNA-1345 D22: Placebo	D1: Flu HD + Placebo D22: mRNA-1345

RSV-A Neutralizing Antibody



Influenza A/H3N2, HAI



GMT; Geometric Mean Titer

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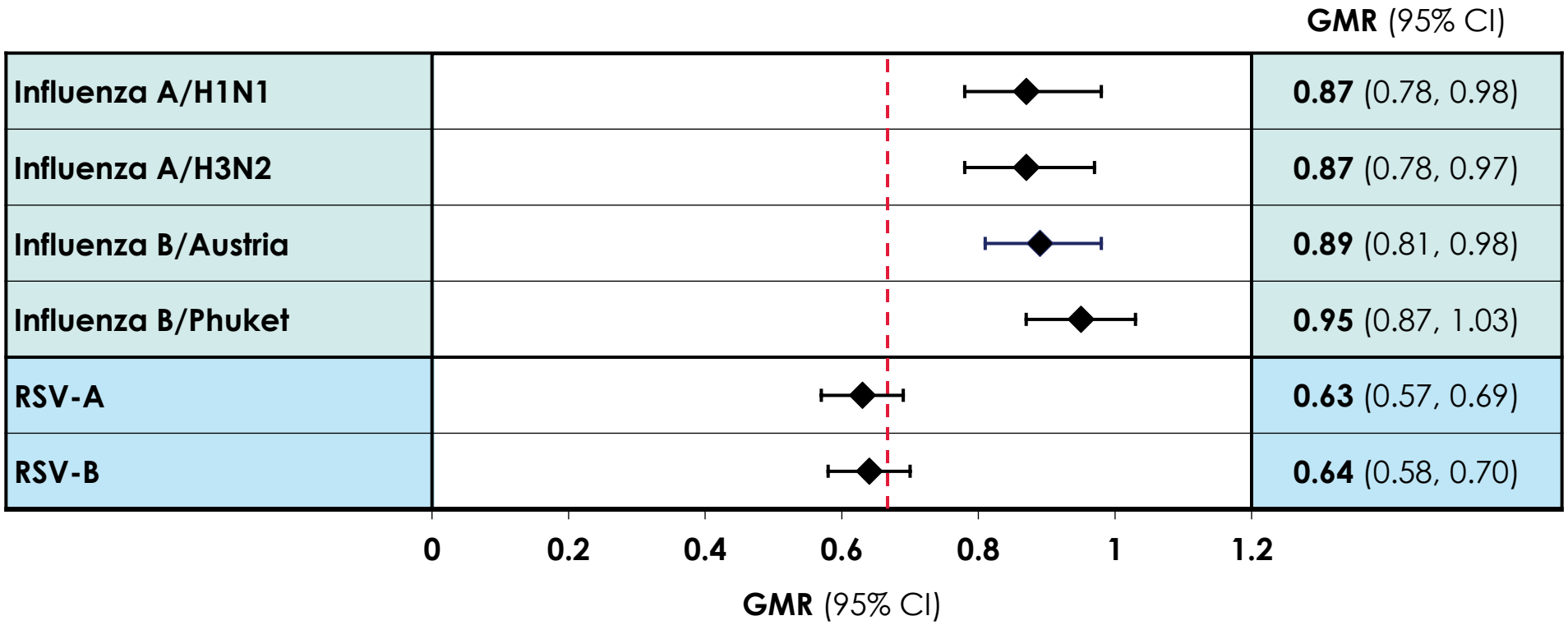
Co-Primary Immunogenicity Endpoint Evaluation

Study 304



GMR for all influenza strains close to 1; RSV GMRs lower, potential for clinical impact on efficacy will be discussed

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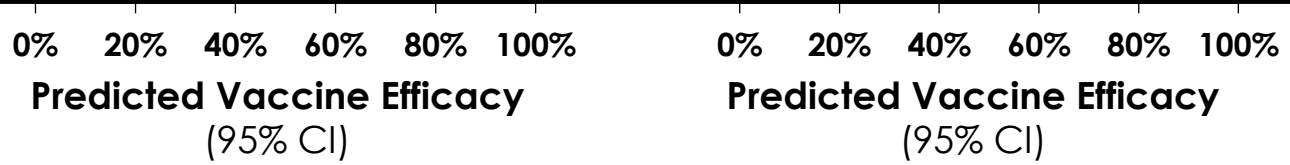
Correlation of Protection Suggests RSV Vaccine Efficacy Maintained with Concomitant Administration of mRNA-1345 and Fluzone HD

Study 304 – Adults ≥65 Years

Antibody	Treatment Group[1]	Day 22 GMT	RSV-LRTD 2+	RSV-LRTD 3+
RSV-A (IU/mL)	Coadministration	11,570	**70%** (54, 84)	**86%** (70, 96)
	Sequential Administration	**19,203**	**77%** (64, 87)	**88%** (75, 97)
RSV-B (IU/mL)	Coadministration	4,036	**69%** (51, 83)	**86%** (69, 97)
	Sequential Administration	**6,876**	**73%** (58, 85)	**88%** (73, 97)



No statistical difference in predicted vaccine efficacy; point estimates were similar

1. Concomitant administration: Fluzone HD + mRNA-1345 at Day 1; Sequential Administration: Fluzone HD + placebo at Day 1, mRNA-1345 at Day 22
Correlate of protection model based on ≥ 65 yr olds in study 301 to be consistent with age of study 304 participants

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Concomitant Administration of mRNA-1345 and Fluzone HD Well Tolerated with No Safety Concerns Identified

Study 304

- **Concomitant administration well tolerated**
  - Predominantly mild events
  - 1-3 days duration

- **Reassuring safety profile:**
  - No Guillain-Barre Syndrome (GBS)
  - No acute disseminated encephalomyelitis (ADEM)
  - No anaphylaxis
  - No thrombocytopenia
  - No cases of acute myocarditis or acute pericarditis

CEAC – Cardiac Event Adjudication Committee

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Concomitant Administration of mRNA-1345 with Standard Dose Influenza and COVID-19 Vaccines

Study 302, Parts A & B

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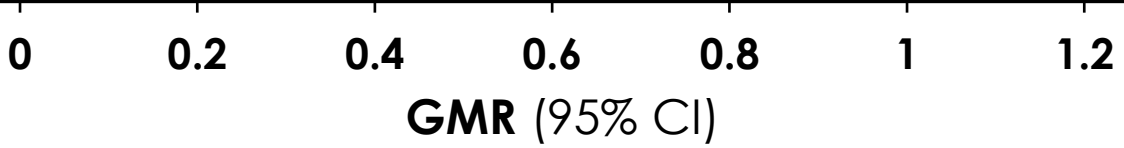
Comparable Immunogenicity with Concomitant vs Nonconcomitant Administration of mRNA-1345 and Standard Dose Influenza Vaccine

Study 302, Part A

Antibody	GMR (95% CI)
Influenza A/H1N1	**0.89** (0.77, 1.03)
Influenza A/H3N2	**0.97** (0.86, 1.09)
Influenza B/Phuket	**0.91** (0.81, 1.02)
Influenza B/Washington	**0.93** (0.82, 1.05)
RSV-A Neutralizing	**0.81** (0.67, 0.97)
RSV-B Neutralizing	**0.85** (0.73, 1.00)



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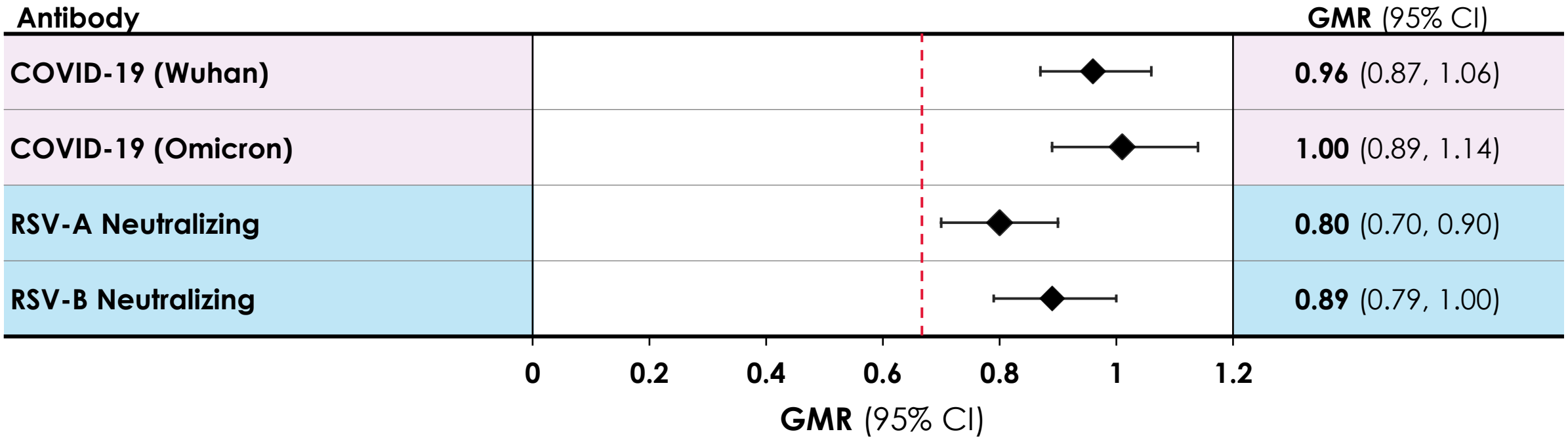
Comparable Immunogenicity with Concomitant vs Nonconcomitant Administration of mRNA-1345 and COVID-19 Bivalent Vaccine

Study 302, Part B



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Thank you

- Investigators
- Study site personnel
- Laboratory personnel
- Most importantly, the individuals who participated in these trials

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