Efficacy and Safety of mRNA-1345, an RSV Vaccine, in Older Adults: Results through ≥6 Months of Follow-up

and

Evaluation of Correlate of Protection Against RSV

February 15, 2024
Presented at the 8th ReSViNET Conference (RSVVW 2024)
Mumbai, India

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Efficacy and Safety of mRNA-1345, an RSV Vaccine, in Older Adults: Results through ≥6 Months of Follow-up

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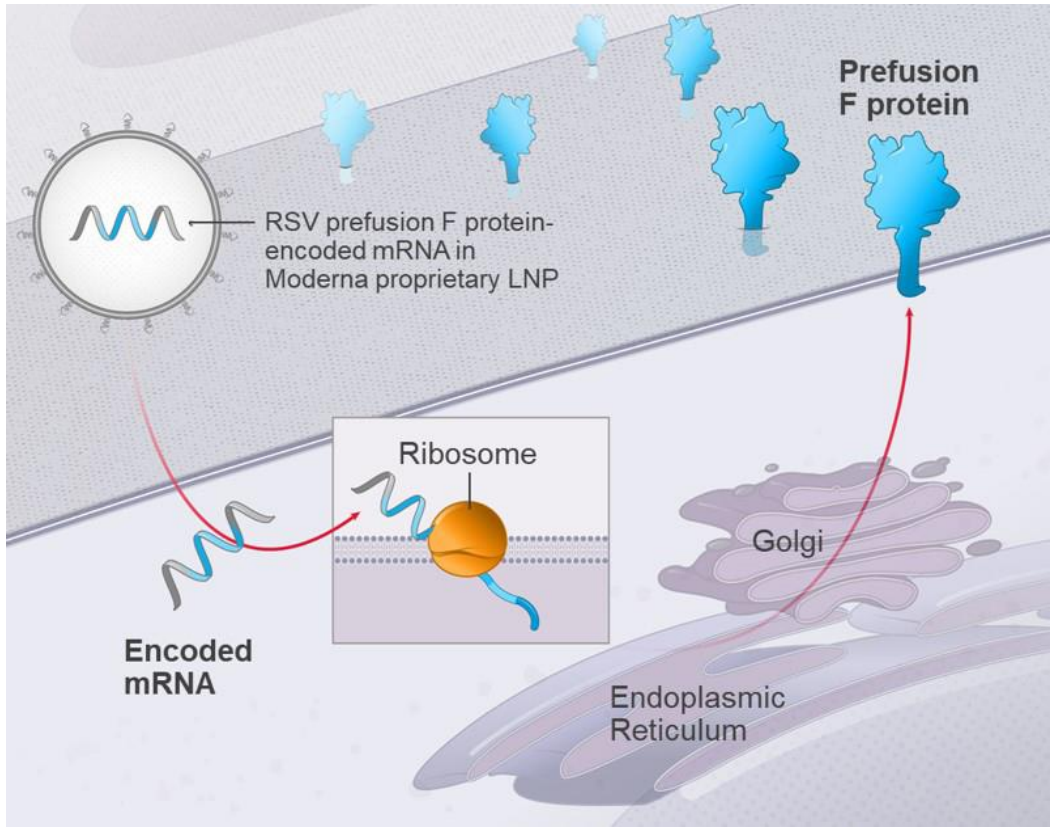
Investigational RSV Vaccine (mRNA-1345) Designed to Encode for a Stabilized Prefusion F Glycoprotein

- LNP encapsulated mRNA-based vaccine encoding the RSV fusion (F) glycoprotein stabilized in the prefusion conformation
- Prefusion F elicits potent neutralizing antibody response[1,2]
- Antibodies to the F protein cross-react between RSV-A and RSV-B
- RSV vaccine uses the same LNP as Moderna COVID-19 vaccines[3]
- Phase 1: mRNA-1345 is well tolerated with persistent antibody levels through 12 months[4]



ARD, acute respiratory disease; F, fusion; LNP, lipid nanoparticle; LRTD, lower respiratory tract disease; mRNA, messenger ribonucleic acid; RSV, respiratory syncytial virus

1. Crank MC, et al. *Science*. 2019;365:505-509. 2. McKekkan JS, et al. *Science*. 2013;342(6158):592-598. 3. Aranda SS and Polack FP. *Front Immunol*. 2019;10:1006. 4. Simorellis A, et al. ESWI 2023.

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mRNA-1345 Pivotal Phase 2/3 Clinical Trial: Population/Study Design

Ongoing phase 2/3, double-blind, placebo-controlled study (NCT05127434) in 22 countries[1]

Population

- Healthy adults including those with chronic, stable medical conditions, and/or frailty
- ≥60 years of age
- 22 countries (both Northern and Southern Hemisphere)

Regimen and follow-up

- Randomized (1:1) to receive single dose vaccination
  - mRNA-1354 50 µg (N=18,304)
  - Saline placebo (N=18,045)
- 24-month follow-up

Stratified by

- Age (60-74 and ≥75 years)
- Presence or absence of congestive heart failure or chronic obstructive pulmonary disease

Individuals with Comorbidities

- COPD
- CHF
- Asthma
- Chronic respiratory disease[a]
- Diabetes
- Advanced liver disease
- Advanced renal disease

[a]Chronic respiratory disease includes chronic pulmonary fibrosis (idiopathic and otherwise), restrictive lung disease, asbestosis, bronchiectasis, cystic fibrosis, pulmonary hypertension, sarcoidosis, and history of tuberculosis.

Frail Individuals

- Measured by Edmonton Frail Scale across 9 domains:
  - Cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, and functional performance
- 0-17 Point scale
  - Fit (0-3)
  - Vulnerable (4-5)
  - Frail (6-17)

ARD, acute respiratory disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; D, day; LRTD, lower respiratory tract disease; M, month; mRNA, messenger ribonucleic acid; RSV, respiratory syncytial virus.

1. ClinicalTrials.gov. NCT05127434. https://clinicaltrials.gov/ct2/show/NCT05127434.

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Key Efficacy Endpoints

Phase 2/3 Safety and Efficacy Study of mRNA-1345

Primary Efficacy Objectives

- Vaccine efficacy to prevent first episode of RSV-LRTD (Lower Respiratory Tract Disease) between 14 days and 12 months post-injection
  - ≥2 signs/symptoms
  - ≥3 signs/symptoms

Key Secondary Efficacy Objectives

- Vaccine efficacy to prevent first episode of RSV-ARD (Acute Respiratory Disease) between 14 days and 12 months post-injection

Exploratory Endpoint

- Vaccine efficacy against RSV-LRTD with shortness of breath was assessed as a surrogate measure of more severe disease

RSV, respiratory syncytial virus

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Definitions of LRTD and ARD

Phase 2/3 Safety and Efficacy Study of mRNA-1345

RT-PCR Confirmed RSV

RSV surveillance was continuous throughout study follow-up

+

RSV Lower Respiratory Tract Disease (LRTD)

New or Worsening of ≥2 or ≥3 of Signs/Symptoms for ≥24 Hours

Tachypnea	Shortness of Breath	Sputum Production	Wheezing and/or rales and/or rhonchi
Hypoxemia	Fever and/ or Cough	Pleuritic Chest Pain	

LRTD cases are a subset of the ARD cases

RSV Acute Respiratory Disease (ARD)

New or Worsening of ≥1 Signs/Symptoms for ≥24 Hours

Sinus Pain	Hoarseness	Stuffy Nose	Tachypnea	Shortness of Breath	Sputum Production	Wheezing
Sore Throat	Runny Nose	Chills	Hypoxemia	Fever	Pleuritic Chest Pain	
				Cough		

RT-PCR, reverse transcription polymerase chain reaction; RSV, respiratory syncytial virus

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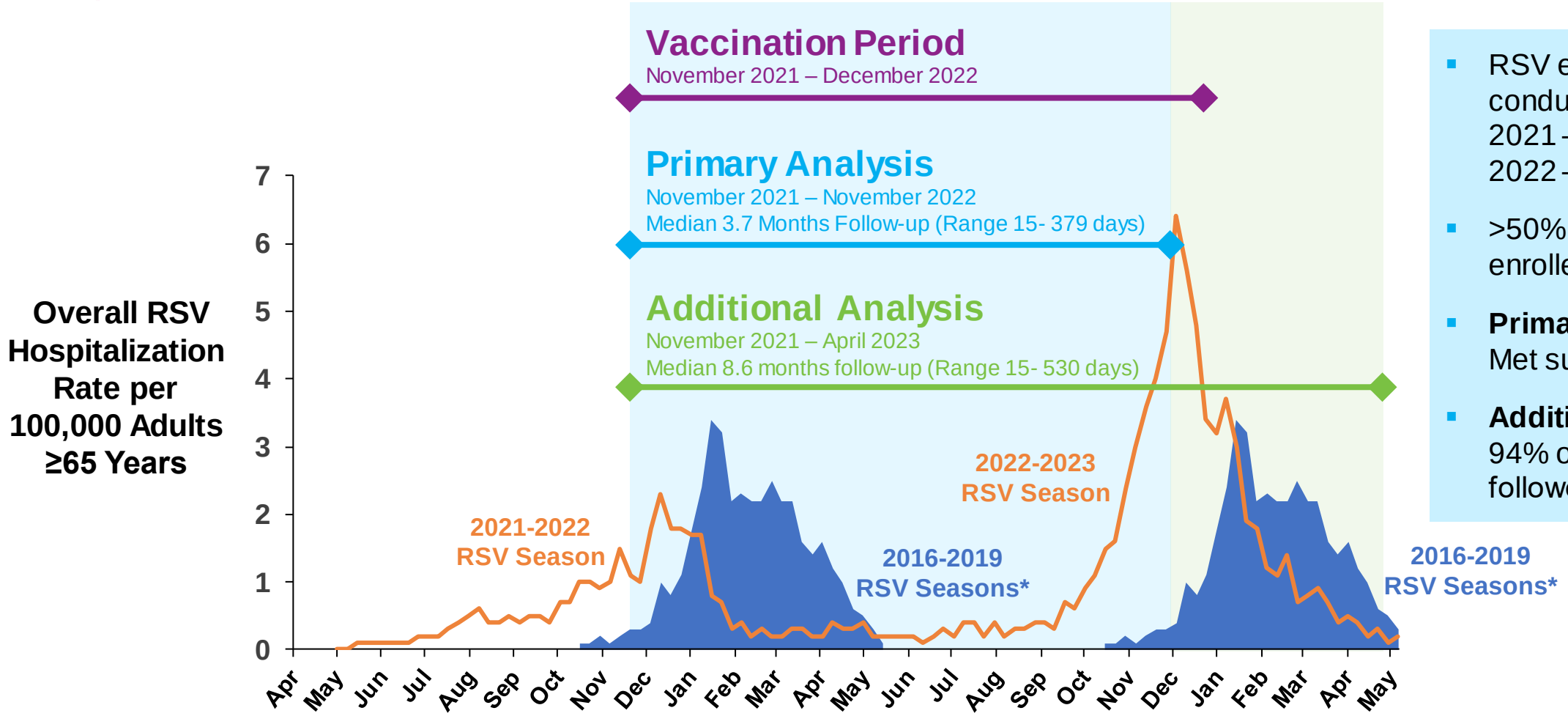
Primary and Additional Efficacy Analyses

US 2021-2023 RSV Hospitalization Rates (RSV-NET) in Adults ≥65 Years[1]



- RSV efficacy study conducted across 2021 – 2022 and 2022 – 2023 seasons
- >50% of participants enrolled in US
- **Primary Analysis:** Met success criteria[2]
- **Additional Analysis:** 94% of participants followed for ≥6 months

*Median RSV hospitalization rate for 2016–2019. Data only collected from October to April each year.

1. CDC. Respiratory Syncytial Virus Hospitalization Surveillance Network (RSV-NET). https://data.cdc.gov/Public-Health-Surveillance/Weekly-Rates-of-Laboratory-Confirmed-RSV-Hospitali/29hc-w46k/data_preview. 2. Wilson E, et al. NEJM. 2023;389:2233-2244.

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Primary Analysis: Vaccine Efficacy for Primary and Key Secondary Endpoints Met Success Criterion (>20% Lower Bound of CI)

Study 301 Per Protocol Analysis, 14 Days – 12 Months After Vaccine/Placebo

	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 17,572)	**Placebo** (N = 17,516)	**Vaccine Efficacy (%) Based on Hazard Ratios[a]**
RSV LRTD ≥2 symptoms	9 (0.05%)	55 (0.31%)	**83.7%** (66.0%, 92.2%)
RSV LRTD ≥3 symptoms	3 (0.02%)	17 (0.10%)	**82.4%** (34.8%, 95.3%)
RSV-ARD	26 (0.15%)	82 (0.47%)	**68.4%** (50.9%, 79.7%)

ARD, acute respiratory disease; LRTD, lower respiratory disease; RSV, respiratory syncytial virus.
Data cutoff for primary analysis was 30 November 2022
[a]Alpha adjusted CI: 95.88% for RSV LRTD ≥ 2 symptoms, 96.36% for RSV LRTD ≥ 3 symptoms, 95.0% for RSV ARD
Wilson et al. NEJM , 2023

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Additional Analysis: Demographics Well-Matched Across Groups; Enrollment Included Those at Highest Risk of Severe RSV (Safety Set)

Characteristic	RSV Vaccine (mRNA-1345) (N = 18,245)	Placebo (N = 18,184)
Median Age, years	**68.5**	**68.5**
60 – 69 years	11,314 **(62%)**	11,253 **(62%)**
70 – 79 years	5,493 **(30%)**	5,482 **(30%)**
≥80 years	1,438 **(8%)**	1,449 **(8%)**
Race, n (%)		
White	11,273 **(62%)**	11,252 **(62%)**
Black or African American	2,160 **(12%)**	2,203 **(12%)**
Ethnicity, n (%)		
Not Hispanic or Latino	11,968 **(66%)**	11,827 **(65%)**
CHF or COPD, n (%)	1,304 **(7%)**	1,310 **(7%)**
≥1 Comorbidity of Interest, n (%)	5,397 **(30%)**	5,289 **(29%)**
Frailty, n (%)		
Vulnerable (score of 4-5)	2,841 **(16%)**	2,907 **(16%)**
Frail (score of 6-17)	1,009 **(6%)**	1,027 **(6%)**

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease

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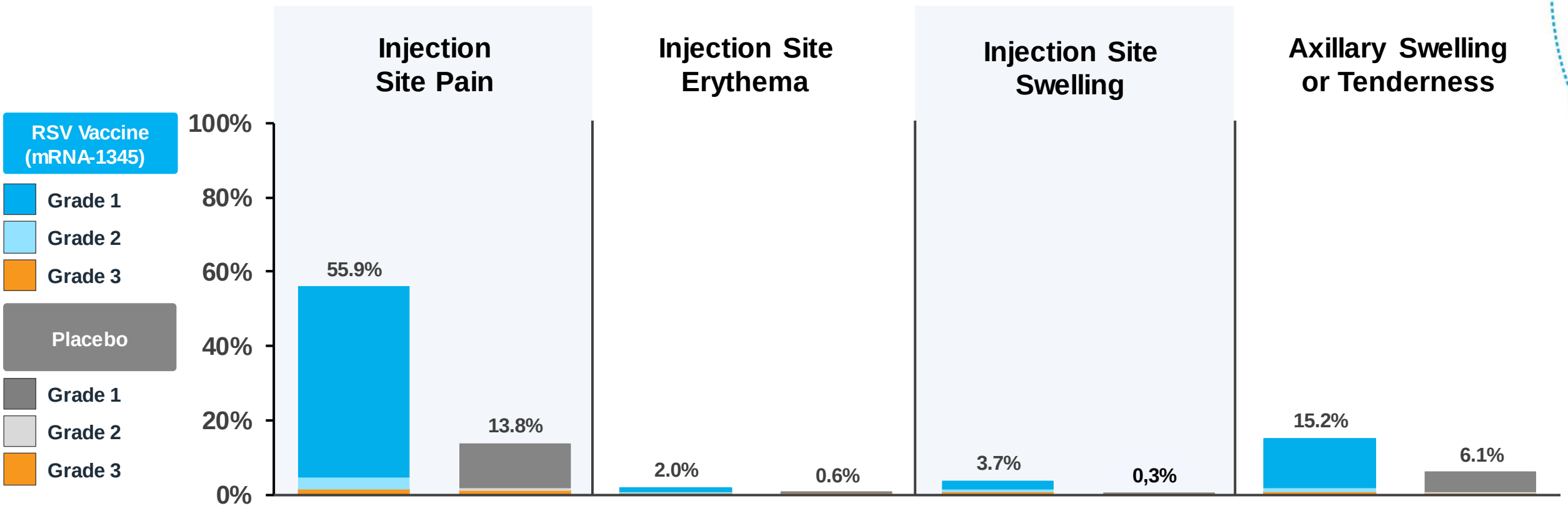
Additional Analysis: Solicited Local Reactions within 7 Days After RSV Vaccine vs Placebo

Study 301 - Solicited Safety Set – Adults ≥60 Years



Mostly grade 1, onset day 1-2, median duration of 1-2 days for RSV vaccine

mRNA-1345 n=18174; placebo, n=18102
Cutoff for additional analysis was 30 April 2023

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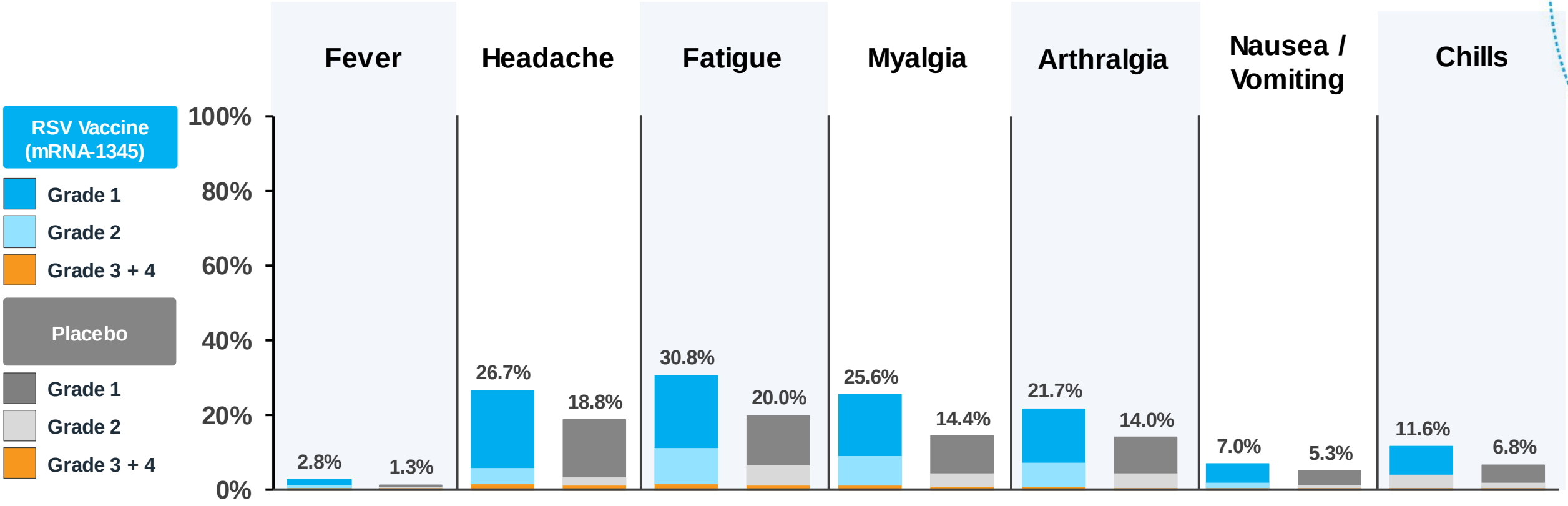
Additional Analysis: Solicited Systemic Reactions within 7 Days After RSV Vaccine vs Placebo

Study 301 - Solicited Safety Set – Adults ≥60 Years



Mostly grade 1, onset day 1-2, median duration of 1-2 days for RSV vaccine

mRNA-1345, n=18174; placebo, n=18102
Grade 4 fever was reported (mRNA-1345 [n=29] and placebo [n=35]); no other categories reported any grade 4 reactions
Cutoff for additional analysis was 30 April 2023

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Unsolicited Adverse Event Within 28 Days After Injection, Regardless of Relationship to Vaccine/Placebo

Study 301 - Solicited Safety Set – Adults ≥60 Years

	RSV Vaccine (mRNA-1345) (N = 18,245)	Placebo (N = 18,184)
All, n (%)	3,749 **(20.5%)**	3,412 **(18.8%)**
Serious	115 **(0.6%)**	111 **(0.6%)**
Fatal	1 **(<0.1%)**	6 **(<0.1%)**
Medically-Attended	1,606 **(8.8%)**	1,531 **(8.4%)**
Leading to Study Discontinuation	2 **(<0.1%)**	11 **(<0.1%)**
Severe/≥Grade 3	129 **(0.7%)**	135 **(0.7%)**
Non-Serious	3,634 **(19.9%)**	3,301 **(18.2%)**
Any Adverse Event of Special Interest (AESI)[a]	3 **(<0.1%)**	8 **(<0.1%)**

No imbalances in any categories between vaccine and placebo recipients

AR, adverse reaction; CEAC, cardiac event adjudication committee; ED, emergency department; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
[a]AESIs were reported up to data cutoff.

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Adverse Events of Special Interest (AESI)

Study 301 – Adults ≥60 Years

- **Neurological Disorders**
  - No cases of Guillain Barre syndrome or acute disseminated encephalomyelitis (ADEM)
  - No imbalance observed for other neurological disorders including Bell's palsy/facial paralysis

- **Cardiac Events**
  - No imbalance observed in cardiac arrhythmias such as atrial fibrillation
  - No CEAC adjudicated cases of:
    - Acute myocarditis in vaccine recipients
    - Acute pericarditis in vaccine recipients with onset <42 days

AR, adverse reaction; CEAC, cardiac event adjudication committee; ED, emergency department; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

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Efficacy of mRNA-1345 Against RSV LRTD and RSV ARD Among Adults ≥60 Years: Additional Analysis (April 30, 2023-Data Cutoff)

Per Protocol Analysis, 14 Days – 12 Months After Vaccine/Placebo

	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 18,112)	Placebo (N = 18,045)	Vaccine Efficacy (%) Based on Hazard Ratios[a]
RSV LRTD ≥2 symptoms	47 (0.26%)	127 (0.70%)	**63.3%** (48.7%, 73.7%)
RSV LRTD ≥3 symptoms	19 (0.10%)	51 (0.28%)	**63.0%** (37.3%, 78.2%)
RSV-ARD	86 (0.47%)	185 (1.03%)	**53.9%** (40.5%, 64.3%)

- **Vaccine protection continues over a longer period (median 8.6 months) through high-transmission '22/'23 RSV season**
- **Lower bound of the confidence interval continued to exceed 20%**

ARD, acute respiratory disease; LRTD, lower respiratory disease; RSV, respiratory syncytial virus.
[a]Alpha adjusted CI: 95.0%

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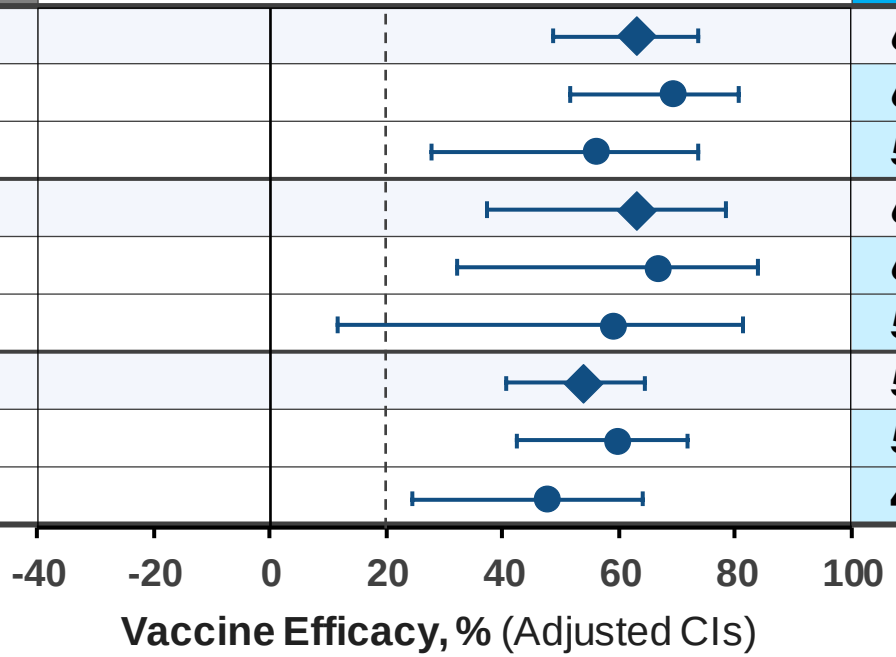
Vaccine Efficacy Against RSV-A and RSV-B by Endpoint Among Adults ≥60 Years – Additional Analysis (April 30, 2023-Data Cutoff)

Per Protocol Analysis, 14 Days – 12 Months After Vaccine/Placebo

		Numbers of Events		Vaccine Efficacy (CI)
		RSV Vaccine (mRNA-1345) (N = 18,112)	Placebo (N = 18,045)	
RSV LRTD ≥2 Symptoms	Overall	47	127	**63.3%** (48.7, 73.7)
	RSV-A	24	78	**69.4%** (51.7, 80.6)
	RSV-B	22	50	**56.3%** (27.9, 73.5)
RSV LRTD ≥3 Symptoms	Overall	19	51	**63.0%** (37.3, 78.2)
	RSV-A	10	30	**66.9%** (32.2, 83.8)
	RSV-B	9	22	**59.3%** (11.7, 81.3)
RSV-ARD	Overall	86	185	**53.9%** (40.5, 64.3)
	RSV-A	43	106	**59.7%** (42.5, 71.7)
	RSV-B	42	80	**47.9%** (24.3, 64.1)



ARD, acute respiratory disease; LRTD, lower respiratory tract disease; mRNA, messenger ribonucleic acid; RSV, respiratory syncytial virus
Black dotted reference line indicates lower bound used to declare success for VE.
One participant in the placebo group presented with RSV-A and RSV-B.

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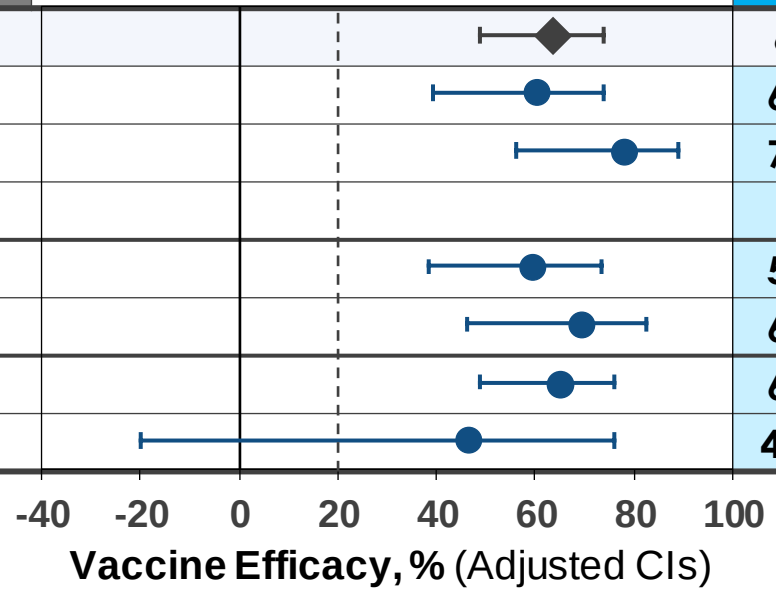
Vaccine Efficacy of mRNA-1345 Against RSV LRTD ≥2 Symptoms Across Subgroups – Additional Analysis (April 30, 2023-Data Cutoff)

Per Protocol Analysis, 14 Days – 12 Months After Vaccine/Placebo

RSV LRTD with ≥2 Symptoms		Numbers of Events: RSV Vaccine (mRNA-1345) (N = 18,112)	Numbers of Events: Placebo (N = 18,045)	Vaccine Efficacy (CI)
Overall		**47**/18,112	**127**/18,045	**63.3%** (48.7, 73.7)
Age	**60–69 Years**	**31**/11,219	**77**/11,170	**60.1%** (39.5, 73.7)
	70–79 Years	**10**/5,464	**45**/5,439	**78.0%** (56.3, 88.9)
	≥80 Years	**6**/1,429	**5**/1,436	**NE**
Comorbidities[a]	**No Comorbidities**	**31**/12,751	**76**/12,796	**59.5%** (38.5, 73.4)
	≥1 Comorbidities	**16**/5,361	**51**/5,249	**69.3%** (46.1, 82.5)
Frailty Status	**Fit** (0-3)	**37**/13,417	**104**/13,274	**65.0%** (49.0, 75.9)
	Vulnerable/Frail (≥4)	**9**/3,817	**17**/3,884	**46.5%** (-20.0, 76.2)



LRTD, lower respiratory tract disease; mRNA, messenger ribonucleic acid; RSV, respiratory syncytial virus
Black dotted reference line indicates lower bound used to declare success for VE.
[a]Comorbidities of interest include COPD, asthma, chronic respiratory disease, diabetes, CHF, advanced liver disease, or advanced renal disease

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Efficacy Against Severe (Based on Shortness of Breath), Medically Attended RSV-LRTD, and Hospitalizations Among Adults ≥60 Years – Additional Analysis

Post Hoc Analysis and Per Protocol Analysis, 14 Days – 12 Months After Vaccine/Placebo

	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 18,112)	Placebo (N = 18,045)	Vaccine Efficacy (%) Based on Hazard Ratios[a]
RSV-LTRD Associated Shortness of Breath[1,2]	11 (0.06%)	43 (0.24%)	**74.6%** (50.7%, 86.9%)
RSV LRTD with ≥2 Symptoms and ER/Urgent Care	5 (0.03%)	13 (0.07%)	**61.8%** (-7.3, 86.4)
RSV Hospitalizations	0 (0%)	2 (0.01%)	**NE**

- Shortness of breath is a key driver of seeking a higher level of care[1,2]
- Vaccine is efficacious in preventing RSV LRTD-associated with shortness of breath
- Vaccine is also efficacious in preventing medically attended RSV-LRTD (ER/urgent care visits)
- 2 hospitalizations in placebo recipients, 0 in vaccine recipients
  - Both participants >70 years with comorbid conditions (asthma); both recovered

ER, emergency room; LRTD, lower respiratory tract disease; mRNA, messenger ribonucleic acid; RSV, respiratory syncytial virus
Based on April 30, 2023 cutoff
[a]95% CI for hazard ratio
1. Falsey et al *NEJM*, 2005; 2. Panozzo et al *ESWI*, 2023

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Conclusions from Additional Analysis

- **mRNA-1345 is well-tolerated; acceptable safety profile in adults aged ≥60 years**
  - No events of Guillain Barre syndrome or acute disseminated encephalomyelitis reported
- **Single dose of mRNA-1345 continued to demonstrate efficacy across spectrum of RSV disease**
  - LRTD with ≥2 or ≥3 symptoms, and ARD
- **Vaccine efficacy generally consistent across RSV-A and RSV-B subtypes, across age groups, frailty status and in participants with pre-existing comorbidities**
  - In ≥80yo, few cases were observed but immunogenicity was found to be consistent *(Poster: Immunogenicity of mRNA-1345: Results from Pivotal Efficacy Trial in Adutls ≥ 60 yrs; Category: Vaccines, Therapies & Treatments)*
- **mRNA-1345 prevented severe RSV disease**
  - Including hospitalization, shortness of breath and medically-attended RSV-LRTD
- **The phase 3 clinical trial of mRNA-1345 in adults aged ≥60 years is ongoing, with additional analyses planned through 24 months**

ARD, acute respiratory disease; LRTD, lower respiratory tract disease; RSV, respiratory syncytial virus

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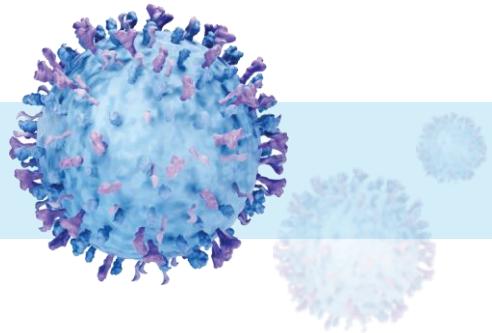
Evaluation of Correlate of Protection Against RSV

Chong Ma, Jiejun Du, Lan Lan, Archana Kapoor, Sanjay Garg, Sonia K. Stoszek, Christine A. Shaw, Jaya Goswami, Eleanor Wilson, Rituparna Das, Honghong Zhou, Lingyi Zheng

Assessment of Correlate of Risk/Protection

Phase 2/3 Safety and Efficacy Study of mRNA-1345

Antibodies have been demonstrated to play a role in protection from RSV in both adults and children[1-4]



- Preplanned case-cohort design for correlates assessment
  - Samples collected on Day 1 (baseline) & 29 from <u>all</u> study participants
  - Assessed immunogenicity (neutralizing antibodies for RSV-A & RSV-B, pre-F binding antibody) in a subset of study participants & all RSV cases according to the sampling plan
    - 1597 vaccine recipients, 533 placebo recipients, 271 RSV cases

Framework for statistics provided by: US Government supported Coronavirus Prevention Network biostatistics and team (David Benkeser, Marco Carone, Youyi Fong, Peter Gilbert, Nima Hejazi, Avi Kenny)

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Case-cohort sampling plan for antibody marker assessment

Case-Cohort Immunogenicity Analysis Set

	Planned Number of participants in per-protocol immunogenicity subset (Total N=1920)*						
Baseline Covariate Strata	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**
mRNA-1345 50 µg	**200**	**200**	**400**	**200**	**200**	**200**	**200**
Placebo	**40**	**40**	**80**	**40**	**40**	**40**	**40**

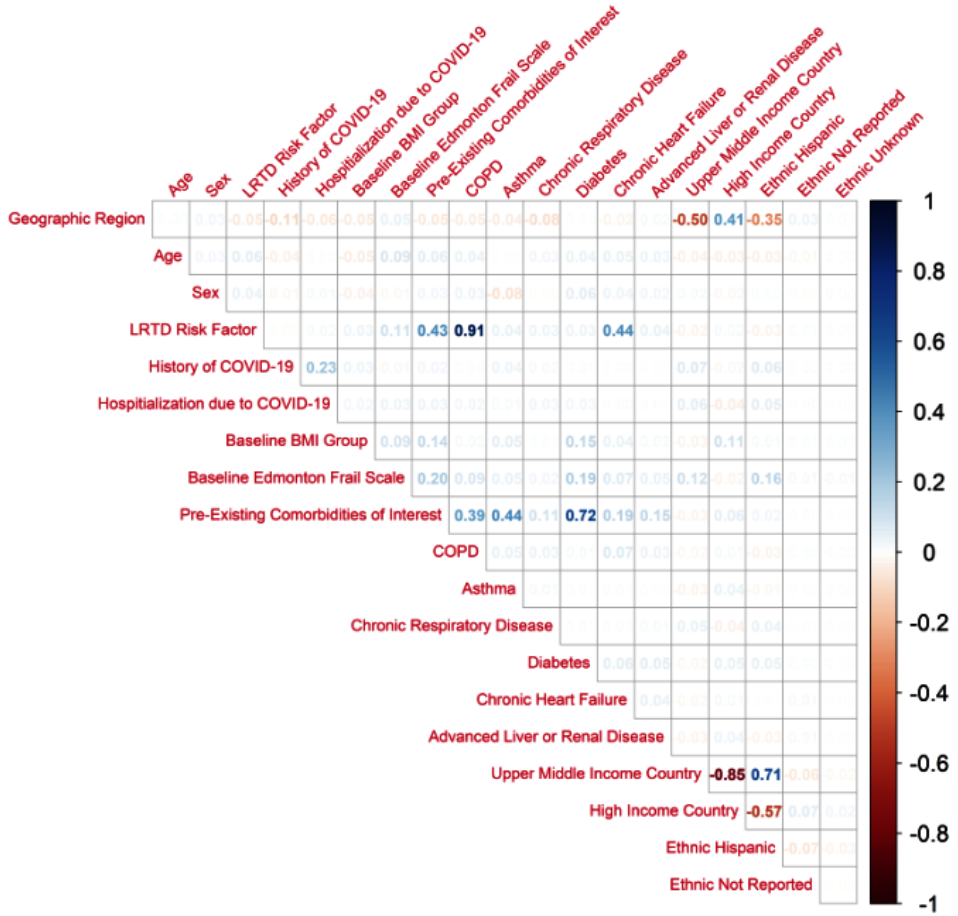
+ **RSV-ARD cases**

Baseline Covariate Strata
S1 = Age 60-74, LRTD risk present, Northern Hemisphere;
S2 = Age 60-74, LRTD risk present, Southern Hemisphere;
S3 = Age ≥75, LRTD risk present (All Regions);
S4 = Age 60-74, LRTD risk absent, Northern Hemisphere;
S5 = Age 60-74, LRTD risk absent, Southern Hemisphere;
S6 = Age ≥75, LRTD risk absent, Northern Hemisphere;
S7 = Age ≥75, LRTD risk absent, Southern Hemisphere.

Efficacy and Safety of mRNA-1345, an RSV Vaccine, in Older Adults: Results through ≥6 Months of Follow-up and Evaluation of Correlate of Protection Against RSV. Presented at RSVVW 2024, Mumbai, India.

RSV Baseline Risk Model

- RSV Baseline risk model was fitted by using the placebo recipients' baseline data
- 17 baseline covariates were preselected for fitting the RSV baseline risk model
- Baseline factors which were correlated were included once in the model



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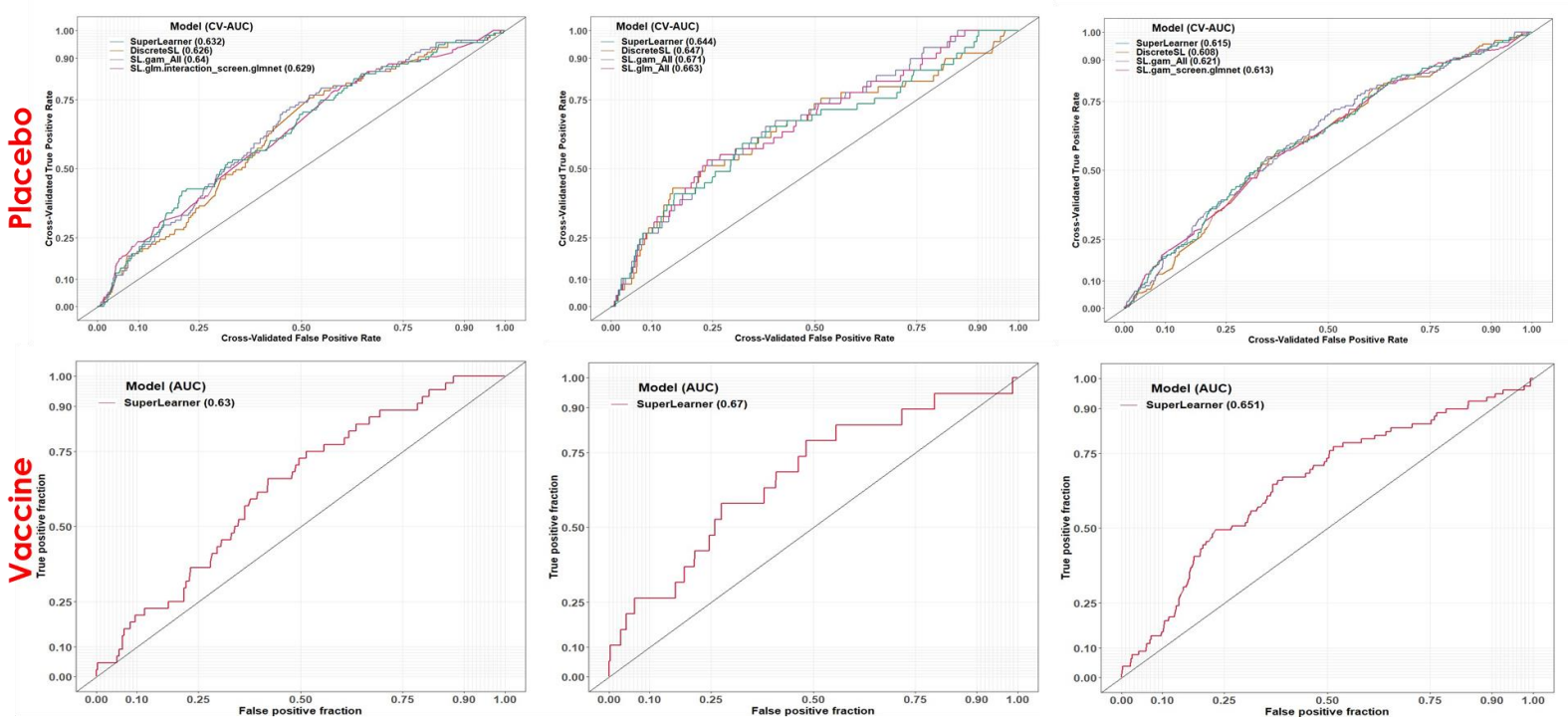
RSV Baseline Risk Model – based on *SuperLearner* (Machine Learning Application)

- The baseline risk model developed using data from the placebo arm only by regressing the outcome of RSVs on preselected baseline covariates
  - 7 learners were used for all eligible baseline covariates and screened baseline covariates to fit the three binary outcome w.r.t RSV-LRTD 2+, RSV-LRTD 3+, RSV-ARD for the placebo recipients
  - The area under ROC curve (AUC) is similar for the placebo recipients and the vaccine recipients



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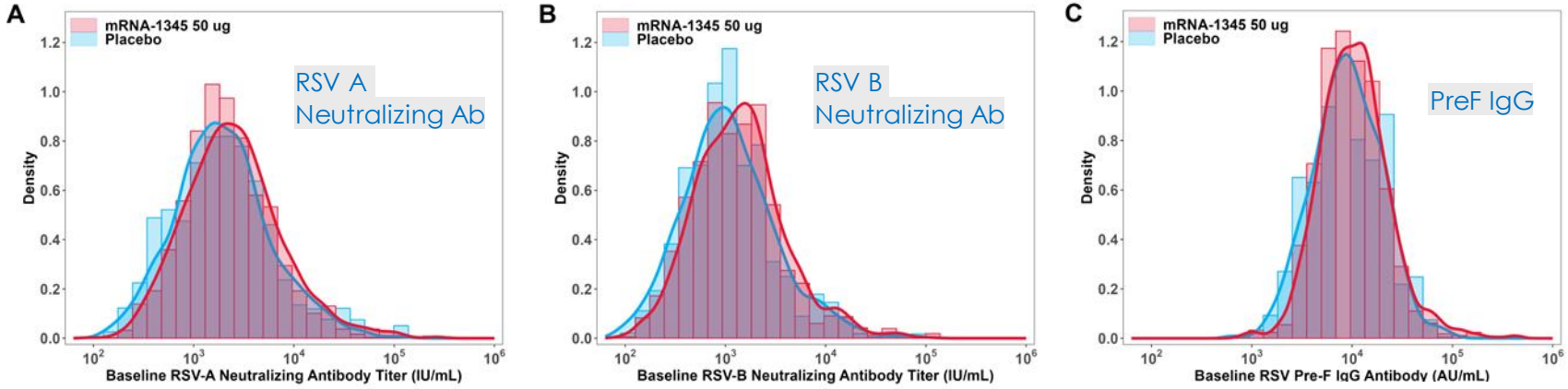
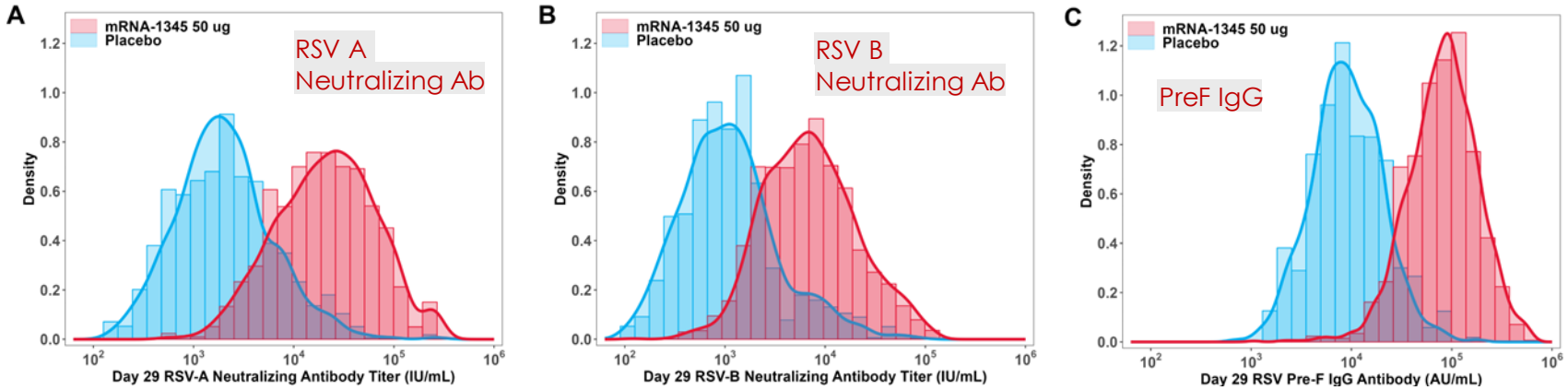
Distribution of Biomarker on D1/D29

Baseline and D29

D1
Distribution of vaccine and placebo arm match



D29
Distribution of vaccine and placebo arm Separated



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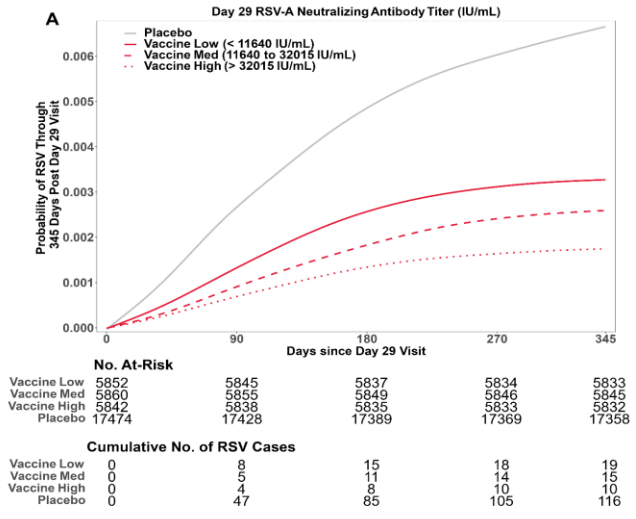
Cumulative Risk for LRTD2+ through 345 Days Post Day 29 Visit by vaccine group and Low/Medium/High RSV-A, RSV-B nAb, PreF IgG bAb concentration

RSV A Neutralizing Ab



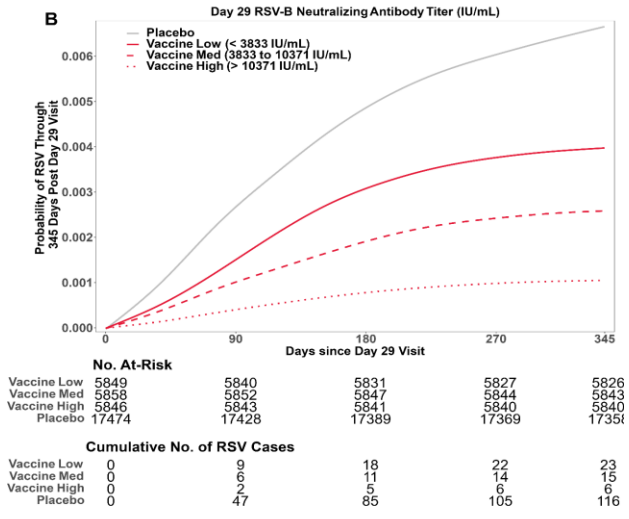
No. At-Risk

Vaccine Low	5852	5845	5837	5834	5833
Vaccine Med	5860	5855	5849	5846	5845
Vaccine High	5842	5838	5835	5833	5832
Placebo	17474	17428	17389	17369	17358

Cumulative No. of RSV Cases

Vaccine Low	0	8	15	18	19
Vaccine Med	0	5	11	14	15
Vaccine High	0	4	8	10	10
Placebo	0	47	85	105	116

RSV B Neutralizing Ab



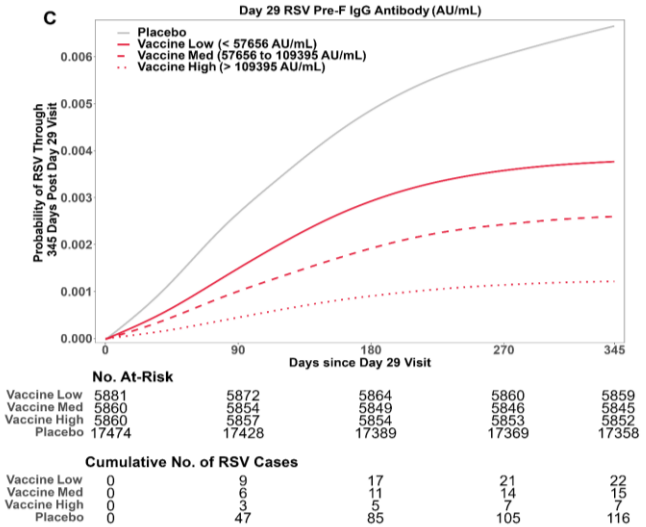
No. At-Risk

Vaccine Low	5849	5840	5831	5827	5826
Vaccine Med	5858	5852	5847	5844	5843
Vaccine High	5846	5843	5841	5840	5840
Placebo	17474	17428	17389	17369	1735(

Cumulative No. of RSV Cases

Vaccine Low	0	9	18	22	23
Vaccine Med	0	6	11	14	15
Vaccine High	0	2	5	6	6
Placebo	0	47	85	105	116

PreF IgG



No. At-Risk

Vaccine Low	5881	5872	5864	5860	5859
Vaccine Med	5860	5854	5849	5846	5845
Vaccine High	5860	5857	5854	5853	5852
Placebo	17474	17428	17389	17369	17358

Cumulative No. of RSV Cases

Vaccine Low	0	9	17	21	22
Vaccine Med	0	6	11	14	15
Vaccine High	0	3	5	7	7
Placebo	0	47	85	105	116

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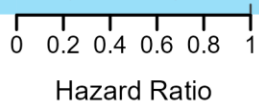
Summary of RSV CoR Models using Day 29 Antibody Markers

A

		Treatment			Day 29 Marker		
Endpoint	Variable Set*	HR (95% CI)	P-value (2-Sided)	FWER-Adjusted P-value	HR (95% CI)	P-value (2-Sided)	FWER-Adjusted P-value
RSV-LRTD 2+	Treatment	0.36 (0.24,0.55)	<0.001	<0.001			
RSV-LRTD 2+	Treatment + RSV-A nAb Titer	0.77 (0.46,1.30)	0.326	0.521	0.44 (0.30,0.65)	<0.001	<0.001
RSV-LRTD 2+	Treatment + RSV-B nAb Titer	0.69 (0.39,1.22)	0.199	0.489	0.42 (0.25,0.72)	0.001	0.002
RSV-LRTD 2+	Treatment + RSV Pre-F IgG Ab	0.82 (0.44,1.51)	0.521	0.521	0.40 (0.23,0.68)	0.001	0.002

*Age, LRTD At-Risk, and baseline risk score are adjusted.



- Day 29 antibody markers correlate with the RSV endpoints (RSV-LRTD 2+ shown)
  - The treatment effect become *insignificant* conditional on the Day 29 marker,
- Day 29 RSV A Neutralizing Ab is a potential CoR/CoP biomarker for all RSV endpoints
- Day 29 RSV Pre-F Binding Ab is also a potential CoR/CoP biomarker for RSV endpoints

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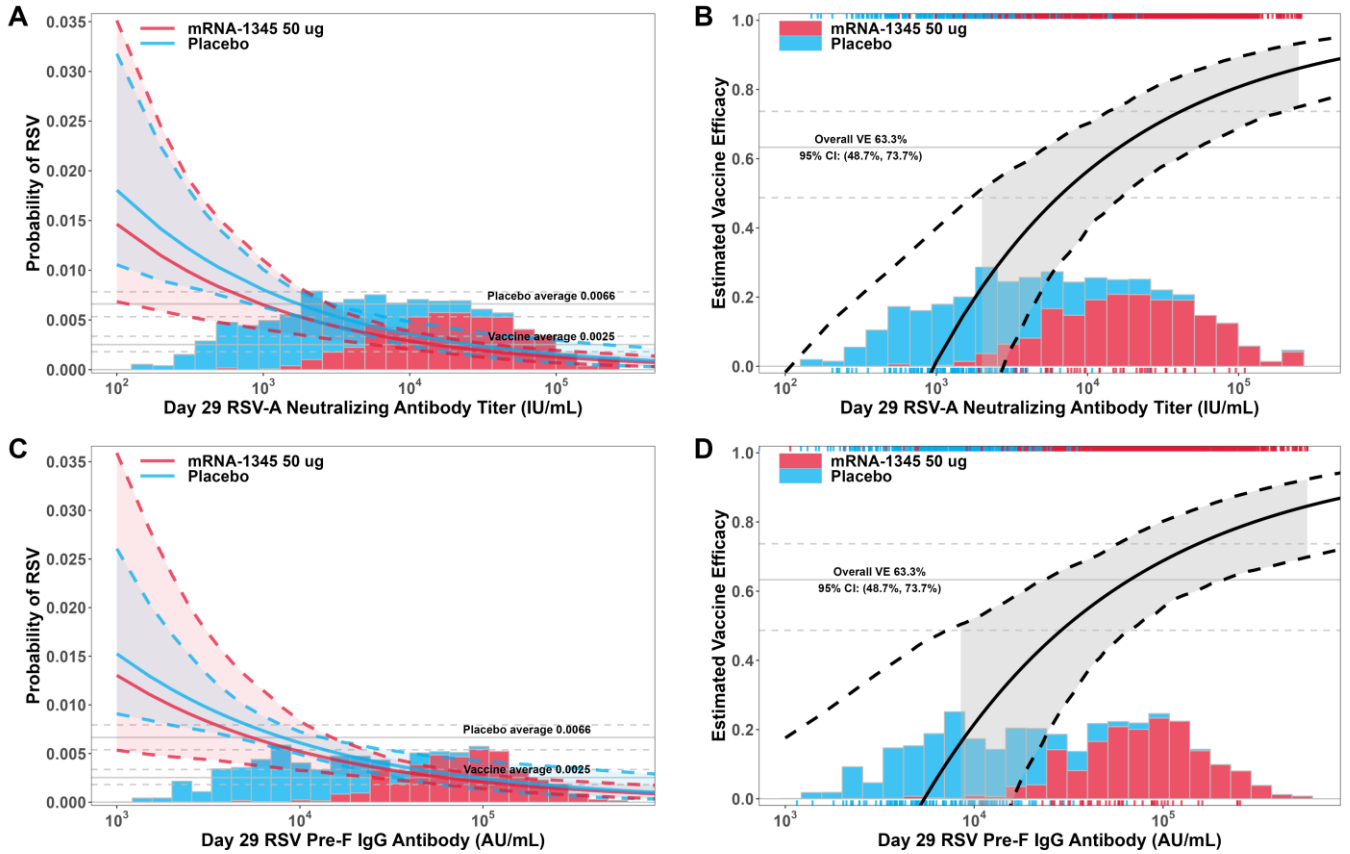
Correlate of Risk and Correlate of Protection – RSV-LRTD 2+

Comparable CVE by Day 29 RSV-A nAb and Day 29 RSV Pre-F IgG Ab

RSV A Neutralizing Ab

PreF IgG



Conclusions:

- Both neutralizing (RSV-A and RSV-B) and binding (pre-F) antibodies at Day 29 correlate with the risk of RSV: the higher the antibody level, the lower the risk of RSV
- RSV-A nAb is a surrogate for RSV vaccine efficacy
- preF binding Ab is also a surrogate for RSV vaccine efficacy

(A-B) and (C-D) demonstrates the further CoR/CoP analysis RSV-LRTD 2+ endpoint by Day 29 RSV-A nAb neutralizing antibody Day 29 RSV Pre-F IgG binding antibody, respectively. (A) and (C): The stacked histogram of the observed antibody marker titers or concentration levels by vaccination status overlayed on the bottom of VE plot. The red and blue solid curves demonstrate the point estimate of the predictive risk for vaccine and placebo recipients at each assigned antibody titer or concentration level. The red and blue dashed curves along with the shades represents the bootstrap point-wise 95% confidence interval. (B) and (D): The solid black curve shows the point estimate of controlled vaccine efficacy at each assigned antibody titer or concentration level, and the dashed curves demonstrate the bootstrap point-wise 95% CI. The rug lines on bottom and top represents the breakthrough cases and the protected non-cases by vaccination status, respectively.

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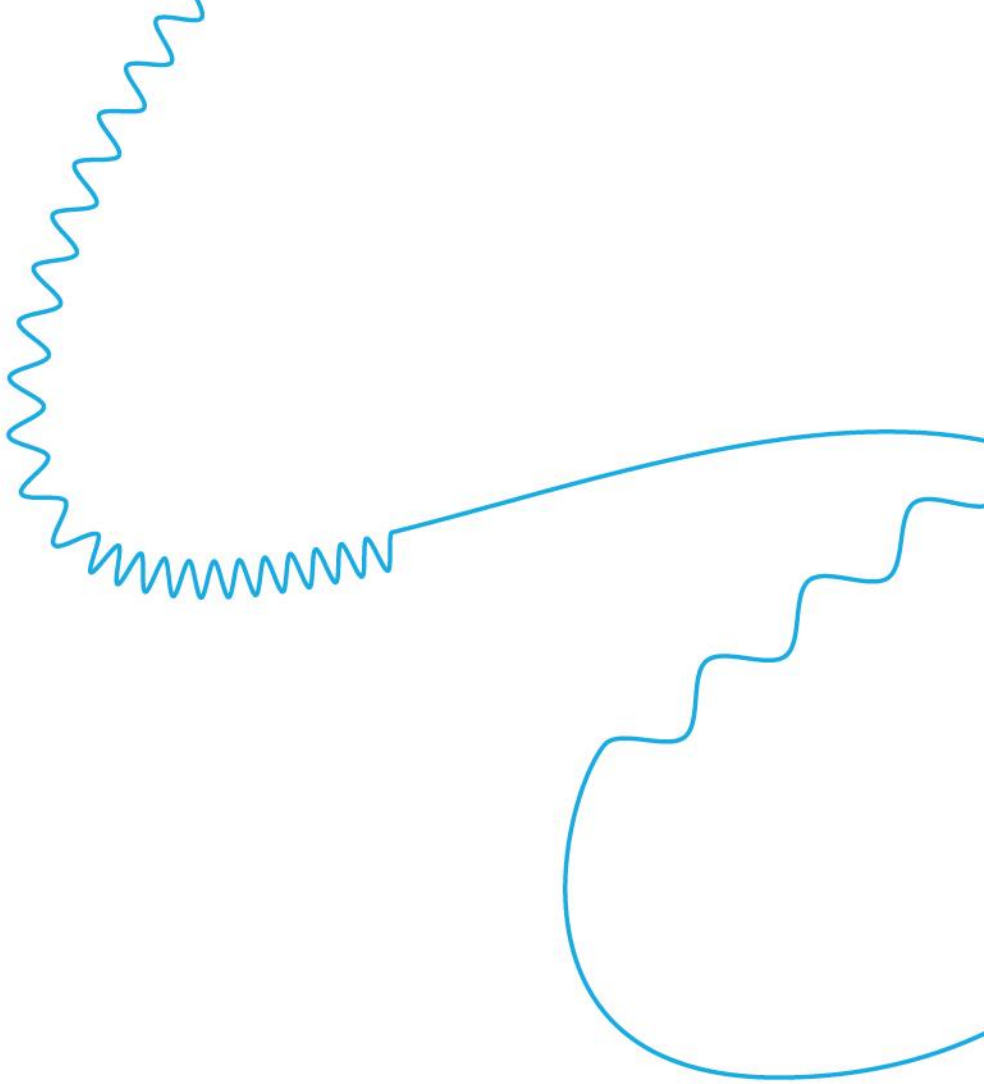
Thank you

- *All investigators and study site personnel*
- *Clinical and laboratory personnel who supported study design and data collection*
- ***Most importantly, the individuals who participated in the trial***

Backups



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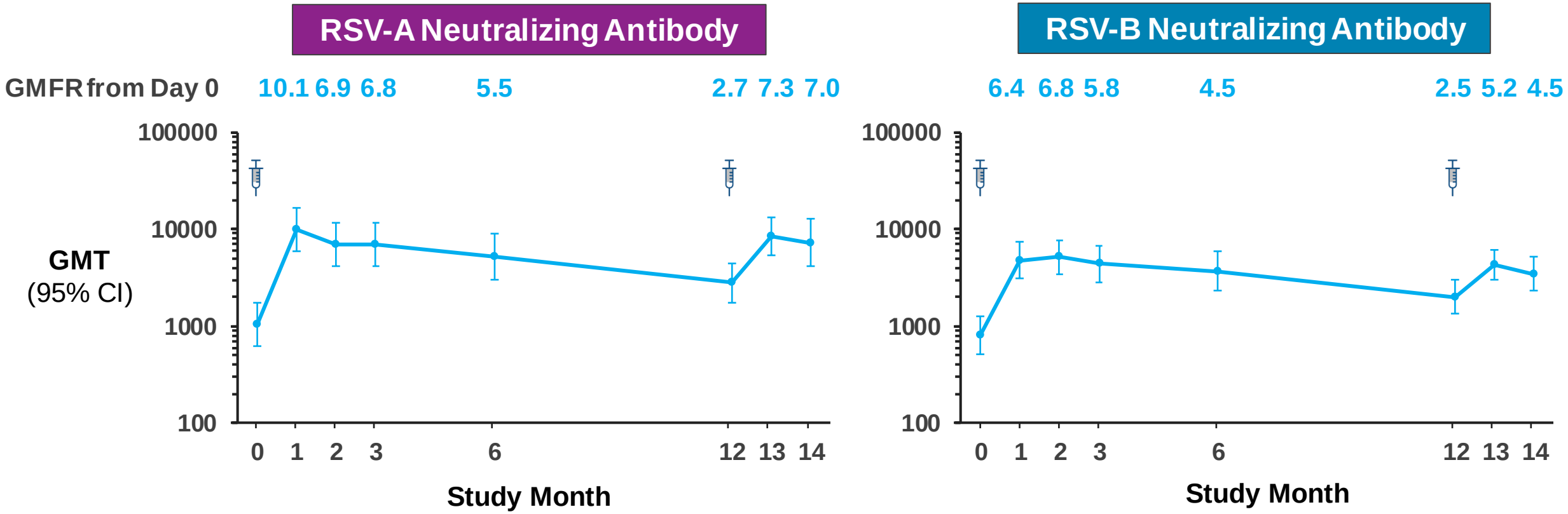
Durability of RSV-A and RSV-B Neutralizing Antibody Response with mRNA-1345 and Revaccination

Study 101 – Adults, 65-79 Years



- RSV-A and RSV-B neutralizing antibodies persist at 12 months post-vaccination, 2-3 fold above baseline
- Revaccination at 12 months results in increase in GMT
- Revaccination at 1 and 2 years is being evaluated in Phase 3 studies

Simorellis et al, *ESWI* 2023