The safety and efficacy of this investigational RSV vaccine have not been established in any country for any use

Overview of Moderna's Investigational RSV Vaccine (mRNA-1345) in Adults ≥ 60 Years of Age

Advisory Committee on Immunization Practices (ACIP)

Rituparna Das, MD, PhD

Feb 29, 2024

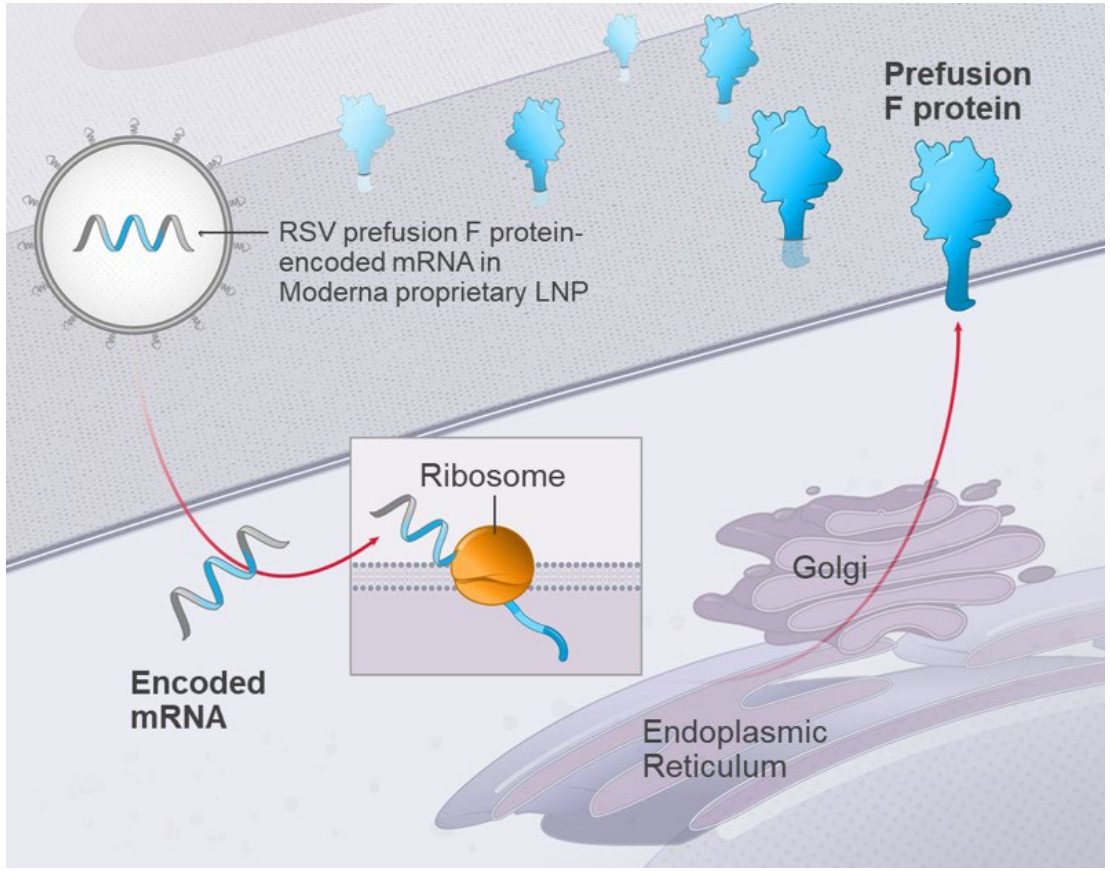
moderna

Outline of Presentation

- Overview of mRNA-1345, Moderna's investigational RSV vaccine
- Pivotal Phase 2/3 trial
  - Efficacy
  - Safety
  - Immunogenicity
- Persistence of antibody and revaccination – Phase 1 trial
- Concomitant administration with influenza and COVID-19 vaccines
- Summary

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]



1. Crank et al. *Science*, 2019; 2. McKekkan et al. *Science,* 2013; 3. Aranda and Polack, *Front Immunol*, 2019; 4. Simorellis et al. *ESWI* 2023

Pivotal Safety and Efficacy Trial of RSV Vaccine, mRNA-1345 (Study 301)

Study Design

Study 301

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

- Single-dose regimen (1:1 50 µg RSV vaccine or saline placebo)
- 24-month follow-up
- Weekly active RSV case surveillance performed throughout study to addresses unpredictability of RSV seasons following pandemic

Stratified by

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

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

Enrollment Enriched for High-Risk Groups

Study 301

Individuals with Comorbidities

- COPD
- CHF
- Asthma
- Chronic respiratory disease[1]
- Diabetes
- Advanced liver disease
- Advanced renal disease

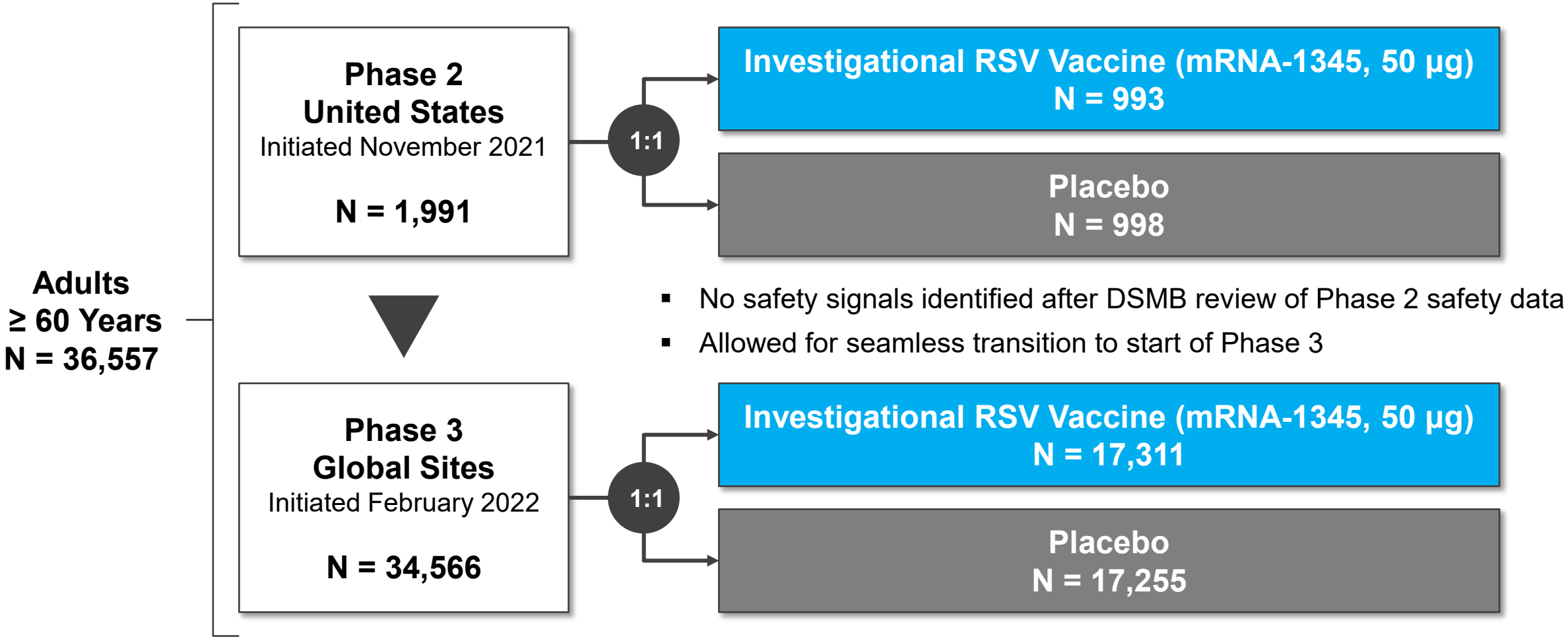
[1] Chronic respiratory disease includes chronic pulmonary fibrosis (idiopathic and otherwise), restrictive lung disease, asbestosis, bronchiectasis, cystic fibrosis, pulmonary hypertension, sarcoidosis, and history of tuberculosis

Frail Individuals

- Measured by Edmonton Frail Scale across 9 domains:
  - Cognition
  - General health status
  - Functional independence
  - Social support
  - Medication use
  - Nutrition
  - Mood
  - Continence
  - Functional performance
- 0-17 point scale
  - Fit (0–3)
  - Vulnerable (4–5)
  - Frail (6-17)

Study Design – Randomization

Study 301



- No safety signals identified after DSMB review of Phase 2 safety data
- Allowed for seamless transition to start of Phase 3

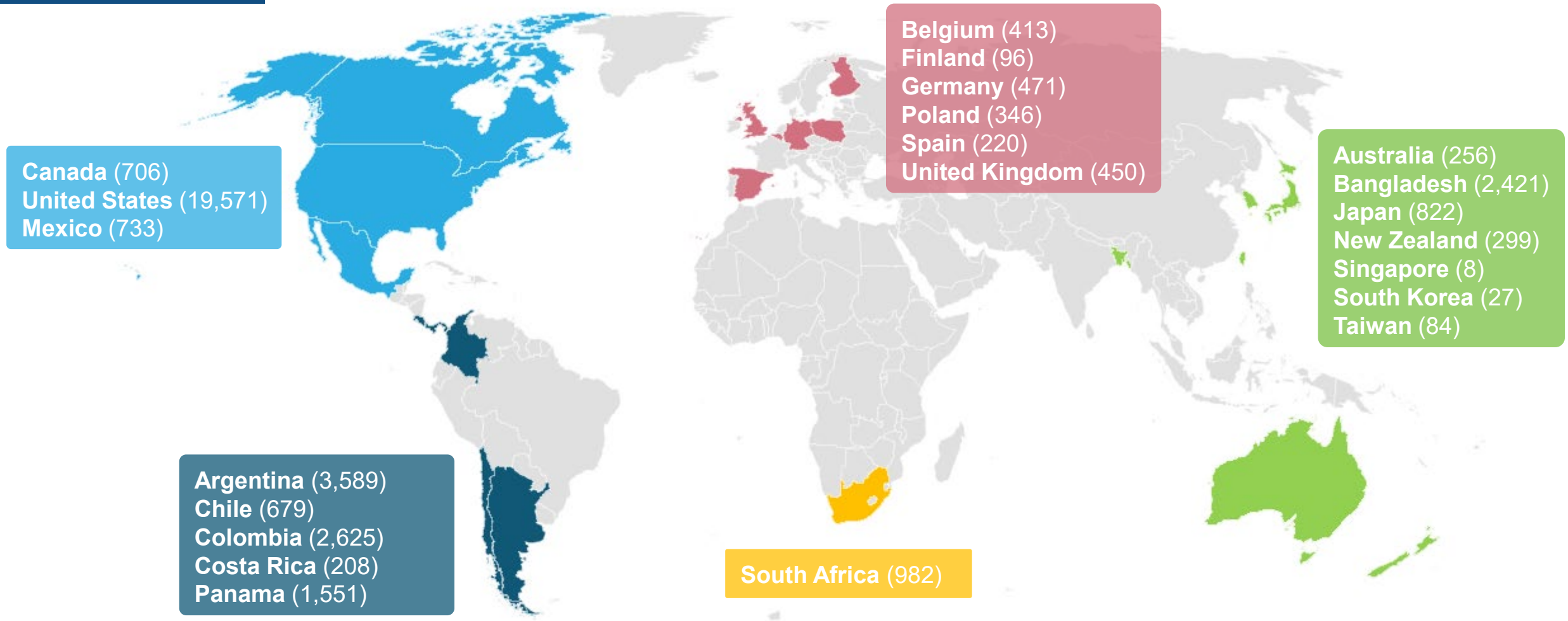
Clinicaltrials.gov NCT05127434 https://clinicaltrials.gov/ct2/show/NCT05127434
DSMB = Data Safety and Monitoring Board

36,557 Participants Enrolled in 22 Countries (as of April 30, 2023 data cutoff)

Study 301

Randomization Set

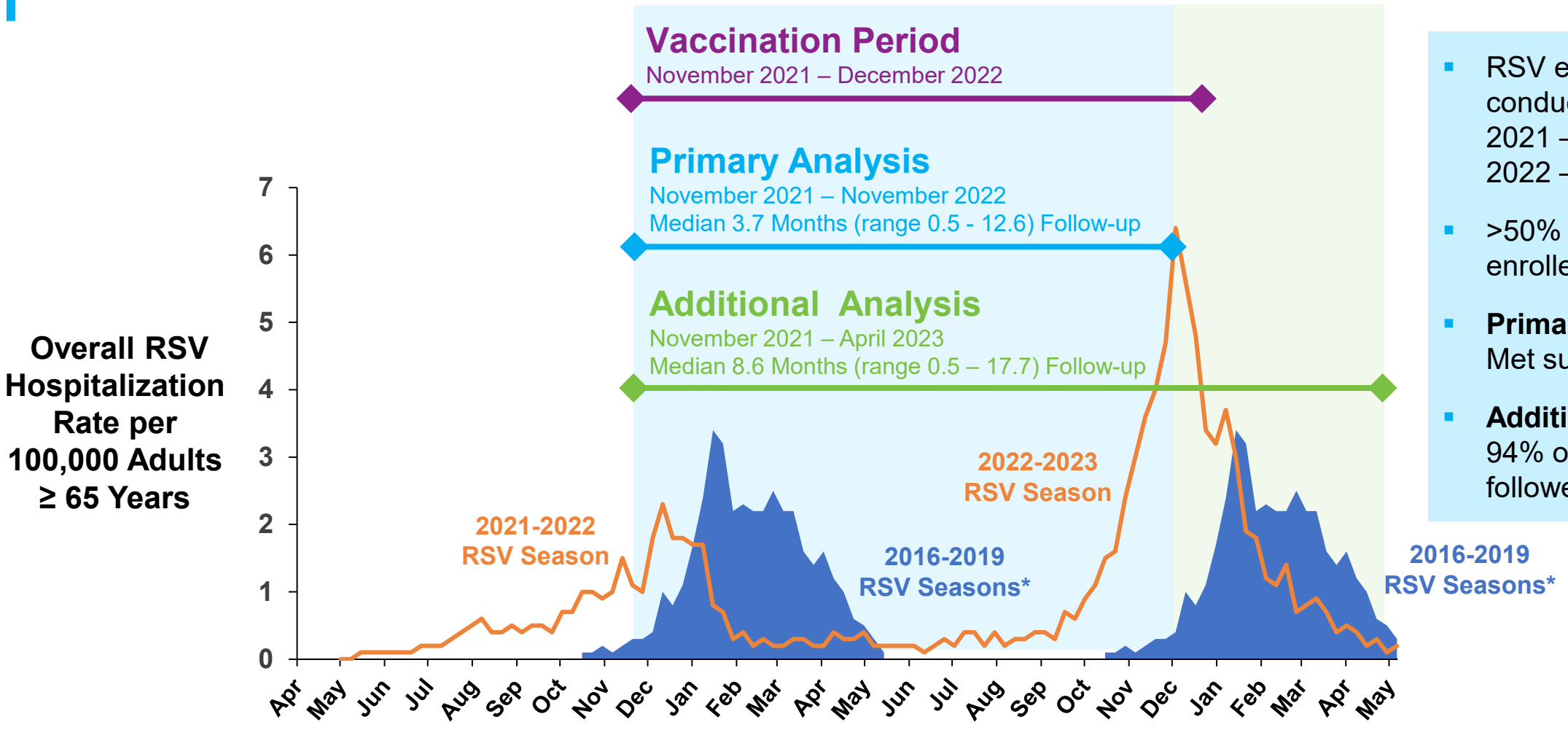
269 Study Sites Across Northern and Southern Hemisphere



Number of participants in each country shown in parentheses

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.

Demographics of Study Participants

Study 301

Randomization Set Characteristic	RSV Vaccine (mRNA-1345) (N = 18,304)	Placebo (N = 18,253)
Median Age, years	**67**	**67**
Male, n (%)	9,376 (**51%**)	9,277 (**51%**)
Age Group, n (%)		
60 – 69 Years	11,348 (**62%**)	11,301 (**62%**)
70 – 79 Years	5,512 (**30%**)	5,500 (**30%**)
≥ 80 Years	1,444 (**8%**)	1,452 (**8%**)
Race/Ethnicity, n (%)		
White	11,318 (**62%**)	11,290 (**62%**)
Black or African American	2,210 (**12%**)	2,175 (**12%**)
Asian	2,014 (**11%**)	2,001 (**11%**)
American Indian or Alaska Native	907 (**5%**)	897 (**5%**)
Native Hawaiian or Other Pacific Islander	28 (**0.2%**)	19 (**0.1%**)
Hispanic / Latino Ethnicity	6,118 (**33%**)	6,169 (**34%**)

Age, gender, race, and ethnicity balanced between vaccine and placebo recipients
Race/ethnicity generally representative of US population

Participants with Lower Respiratory Tract Disease (LRTD) Risk Factors and Comorbidities of Interest

Study 301

Randomization Set

Characteristic	RSV Vaccine (mRNA-1345) (N = 18,304)	Placebo (N =18,253)
CHF or COPD, n (%)	1,310 **(7%)**	1,316 **(7%)**
≥1 Comorbidity of Interest, n (%) COPD, CHF, asthma, chronic respiratory disease[1], diabetes, advanced liver disease, advanced renal disease	5,417 **(30%)**	5,316 **(29%)**
Frailty[2], n (%)		
Vulnerable (score of 4-5)	2,852 **(16%)**	2,917 **(16%)**
Frail (score of 6-17)	1,013 **(6%)**	1,033 **(6%)**

Enrollment included those at highest risk of severe RSV

1. Chronic respiratory disease includes chronic pulmonary fibrosis (idiopathic and otherwise), restrictive lung disease, asbestosis, bronchiectasis, cystic fibrosis, pulmonary hypertension, sarcoidosis, and history of tuberculosis
2. Based on 17-point Edmonton Frailty Score

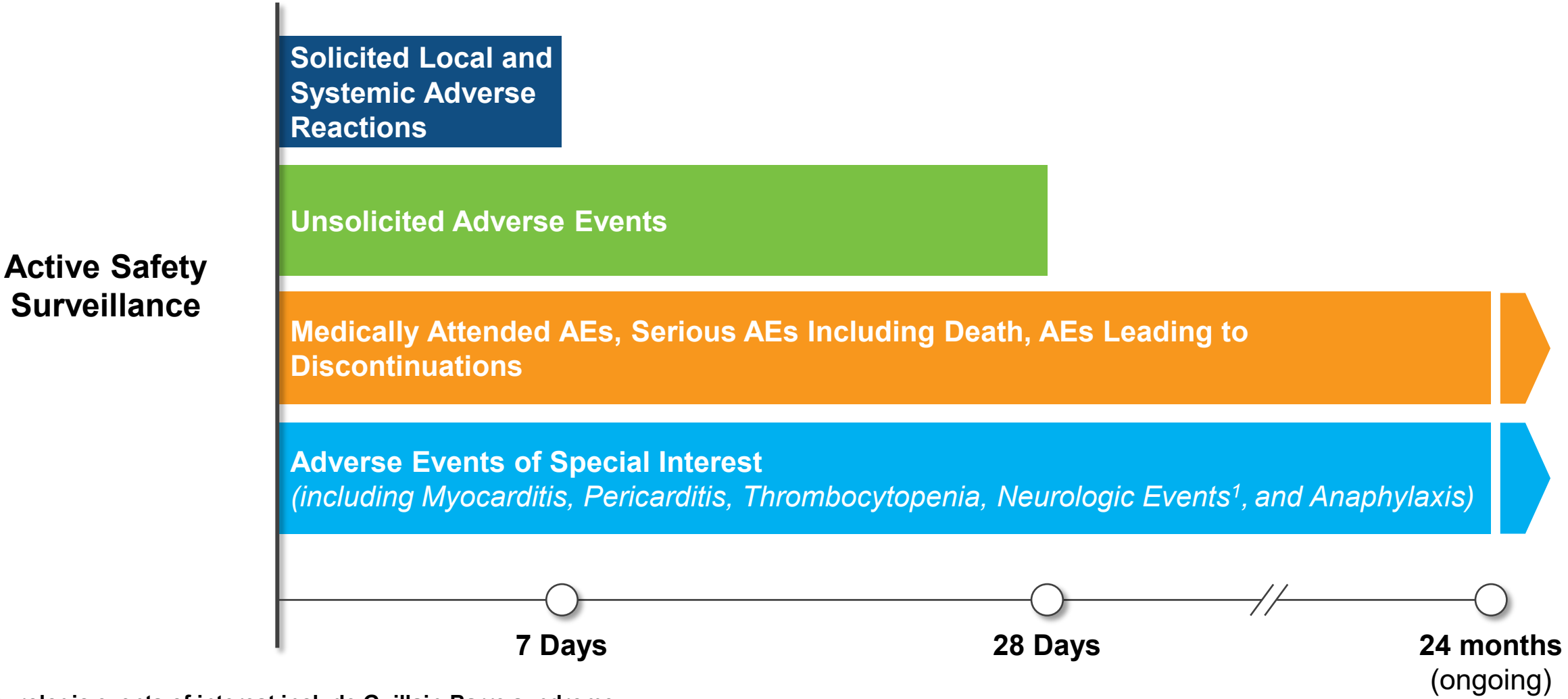
Safety Data
Study 301

Safety Set – April 30, 2023 data cutoff

Based on 6 months of follow-up for ~94% of participants

Primary Safety Endpoints and Duration of Follow-up

Study 301

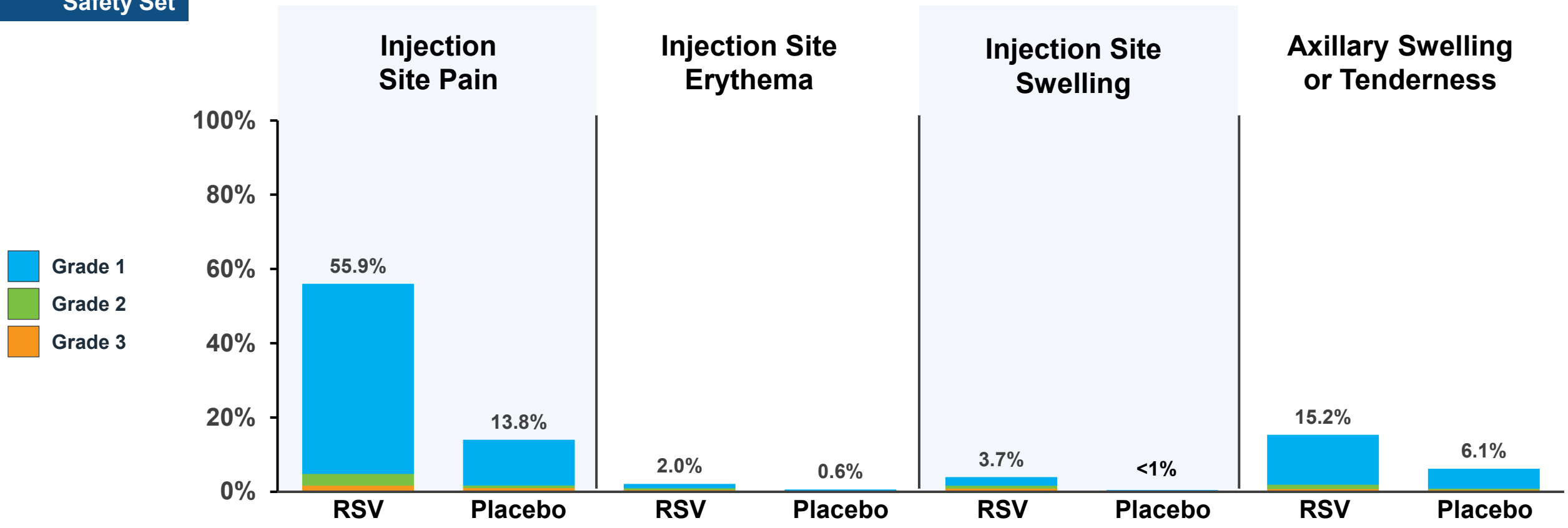


1. Neurologic events of interest include Guillain-Barre syndrome, acute disseminated encephalomyelitis, Bell's palsy, and seizures

Solicited Local Reactions within 7 Days After RSV Vaccine vs Placebo

Study 301 - Solicited Safety Set

Safety Set



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

RSV vaccine, n=18174; placebo, n=18102

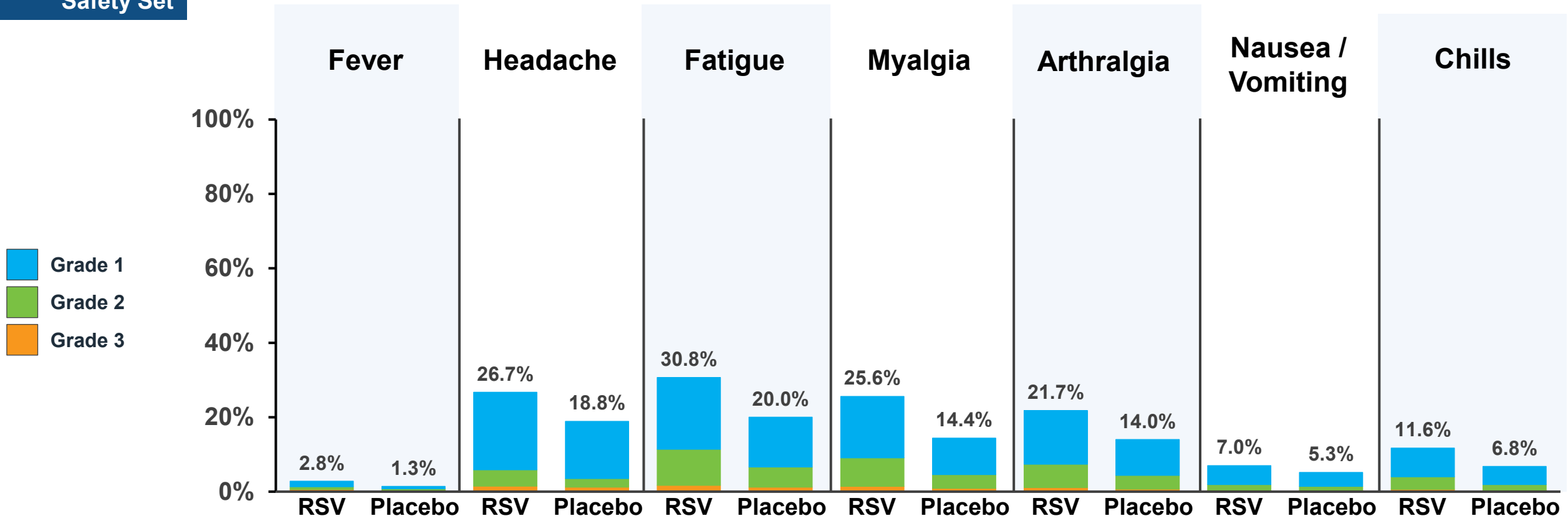
For placebo, grade 2 erythema and grade 2 and grade 3 swelling were < 1%

No grade 4 local adverse reactions

Solicited Systemic Reactions within 7 Days After RSV Vaccine vs Placebo

Study 301 - Solicited Safety Set

Safety Set



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

RSV vaccine, 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

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

Study 301 - Solicited Safety Set

Safety Set	RSV Vaccine (mRNA-1345) (N = 18,245)	Placebo (N = 18,184)
All, n (%)	3,749 **(21%)**	3,412 **(19%)**
Serious	115 **(0.6%)**	111 **(0.6%)**
Fatal	1 **(<0.1%)**	6 **(<0.1%)**
Medically-Attended	1,606 **(9%)**	1,531 **(8%)**
Leading to Study Discontinuation	2 **(<0.1%)**	11 **(<0.1%)**
Severe/≥ Grade 3	129 **(0.7%)**	135 **(0.7%)**
Non-Serious	3,634 **(20%)**	3,301 **(18%)**
Any Adverse Event of Special Interest (AESI)	3 **(<0.1%)**	8 **(<0.1%)**

No imbalances in any categories between vaccine and placebo recipients

Based on April 30, 2023 cutoff

Adverse Events of Special Interest (AESI)

Study 301

Safety Set

- **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

CEAC – Cardiac Event Adjudication Committee
Based on April 30, 2023 cutoff

Efficacy

Study 301

Key Efficacy Endpoints

Study 301

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
- First hospitalization associated with RSV-ARD or RSV-LRTD between 14 days and 12 months post-injection

Exploratory Endpoint

Vaccine efficacy against RSV-LRTD with shortness of breath (a surrogate measure of more severe disease)[1, 2]

1. Falsey et al *NEJM*, 2005; 2. Panozzo et al *ESWI*, 2023

Definitions of LRTD and ARD

Study 301

RT-PCR Confirmed RSV +

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 / Cough	Pleuritic Chest Pain	

RSV surveillance was conducted year-round throughout study follow-up

Primary Analysis

Study 301

Per Protocol Analysis – November 30, 2022 data cutoff

Efficacy of mRNA-1345 Against RSV LRTD and RSV ARD among Adults ≥ 60 Years

Study 301 - Per Protocol Analysis

Primary Analysis

	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 17,572)	Placebo (N = 17,516)	Vaccine Efficacy (%) Based on Hazard Ratios[1]
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%)

- Vaccine efficacy for primary and key secondary endpoints (median 3.7 months) met lower bound of CI criterion (>20%)
- Regulatory criteria for licensure met

1. Alpha adjusted CI: 95.88% for RSV LRTD ≥ 2 symptoms, 96.36% for RSV LRTD ≥ 3 symptoms, 95.0% for RSV ARD

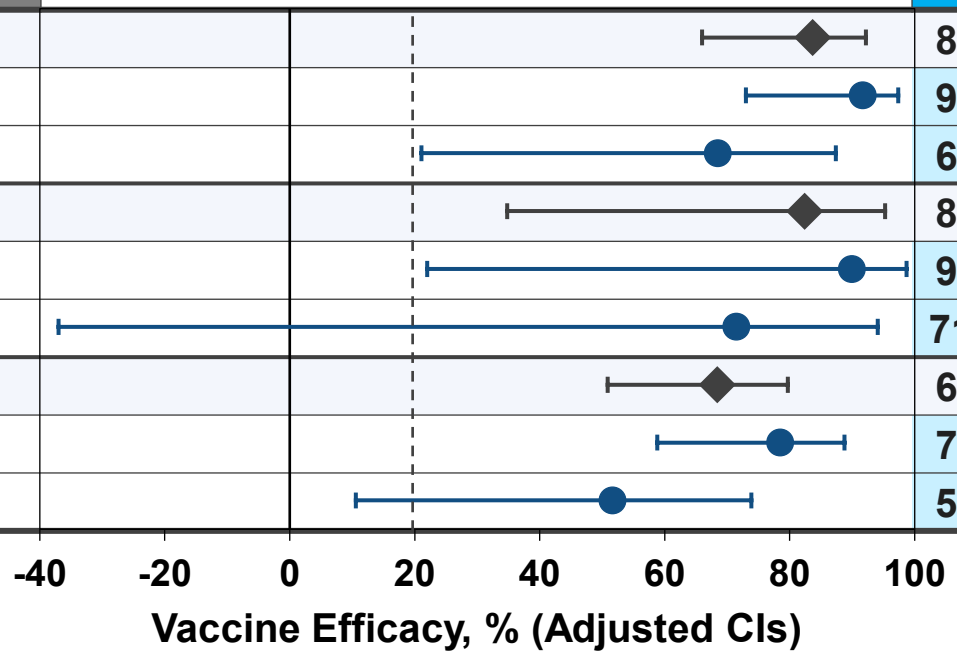
Wilson et al. *NEJM,* 2023

Vaccine Efficacy Against RSV-A and RSV-B by Endpoint

Study 301 - Per-Protocol Efficacy Set

Primary Analysis

		Numbers of Events		Vaccine Efficacy (CI)
		RSV Vaccine (mRNA-1345) (N = 17,572)	Placebo (N = 17,516)	
RSV LRTD ≥ 2 Symptoms	Overall	9	55	**83.7%** (66.0, 92.2)
	RSV-A	3	36	**91.7%** (73.0, 97.4)
	RSV-B	6	19	**68.5%** (21.1, 87.4)
RSV LRTD ≥ 3 Symptoms	Overall	3	17	**82.4%** (34.8, 95.3)
	RSV-A	1	10	**90.0%** (22.0, 98.7)
	RSV-B	2	7	**71.5%** (-37.0, 94.1)
RSV-ARD	Overall	26	82	**68.4%** (50.9, 79.7)
	RSV-A	11	51	**78.5%** (58.8, 88.8)
	RSV-B	15	31	**51.7%** (10.6, 73.9)



- Efficacy was observed for both RSV-A and RSV-B
- Fewer cases of LRTD ≥ 3 symptoms resulted in larger confidence intervals for both subtypes

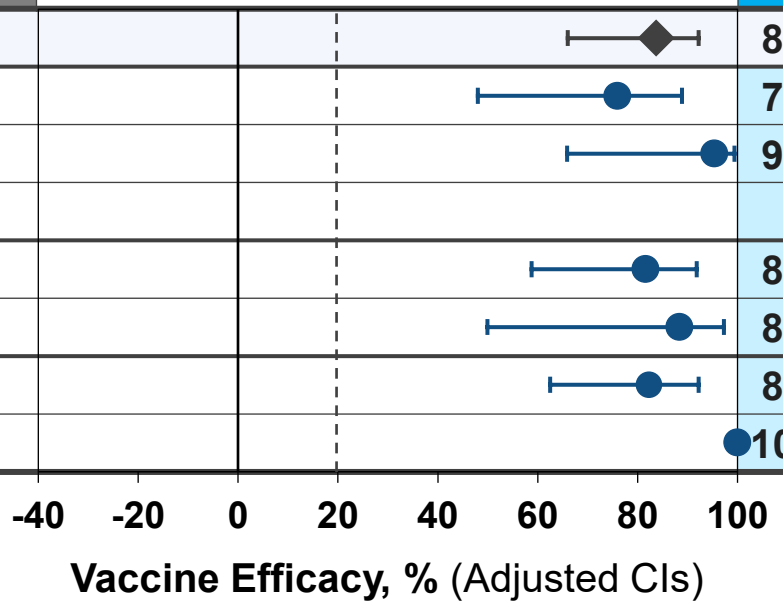
Wilson et al. *NEJM*, 2023

Vaccine Efficacy by Age, Comorbidities, and Frailty Against RSV LRTD ≥ 2 Symptoms

Study 301 - Per-Protocol Efficacy Set

Primary Analysis

RSV LRTD with ≥ 2 Symptoms		Numbers of Events: RSV Vaccine (mRNA-1345) (N = 17,572)	Numbers of Events: Placebo (N = 17,516)	Vaccine Efficacy (CI)
Overall		**9** / 17,572	**55** / 17,516	**83.7%** (66.0, 92.2)
Age	**60 – 69 Years**	**8** / 11,168	**33** / 11,118	**76.0%** (48.0, 88.9)
	70 – 79 Years	**1** / 5,440	**22** / 5,416	**95.4%** (65.9, 99.4)
	≥ 80 Years	**0** / 964	**0** / 982	–
Comorbidities	**No Comorbidities**	**7** / 12,377	**38** / 12,431	**81.6%** (58.8, 91.8)
	≥ 1 Comorbidities	**2** / 5,195	**17** / 5,085	**88.4%** (49.9, 97.3)
Frailty Status	**Fit** (0-3)	**8** / 13,396	**45** / 13,250	**82.3%** (62.5, 91.7)
	Vulnerable/Frail (≥ 4)	**0** / 3,781	**6** / 3,858	**100.0%** (NE, 100.0)



- Case splits favorable for mRNA-1345 with respect to age, comorbidities, and frailty
- No cases observed in ≥ 80-year-olds

Wilson et al. NEJM, 2023; **NE - nonestimable**

Comorbidities include COPD, CHF, asthma, chronic respiratory disease, diabetes, advanced liver disease, advanced renal disease

Efficacy Against Severe (based on Shortness of Breath) and Medically Attended LRTD Among Adults ≥ 60 Years

Study 301 - Post Hoc Analysis/Per Protocol Analysis

Post Hoc Analysis

	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 17,572)	**Placebo** (N = 17,516)	**Vaccine Efficacy (%) Based on Hazard Ratios (95% CI)**
RSV-LRTD Associated Shortness of Breath[1,2]	2 (0.01%)	15 (0.09%)	**86.7%** (41.9%, 97.0%)
Medically Attended RSV-LRTD (≥ 2 Symptoms and ER/Urgent Care)	0	5 (0.03%)	**NE**

- Shortness of breath is a key driver of seeking a higher level of care[1,2]
- Vaccine is efficacious in preventing shortness of breath associated with RSV-LRTD
- Case split favorable for medically attended RSV-LRTD (ER/urgent care visits)

Based on Nov 30, 2022 cutoff; NE - nonestimable

1. **Falsey et al *NEJM,* 2005; 2. Panozzo et al. *ESWI*, 2023**

Additional Analysis

Study 301

Per Protocol Analysis – April 30, 2023 data cutoff

Efficacy of mRNA-1345 Against RSV LRTD and RSV ARD among Adults ≥ 60 Years

Study 301 - Per Protocol Analysis

Additional Analysis

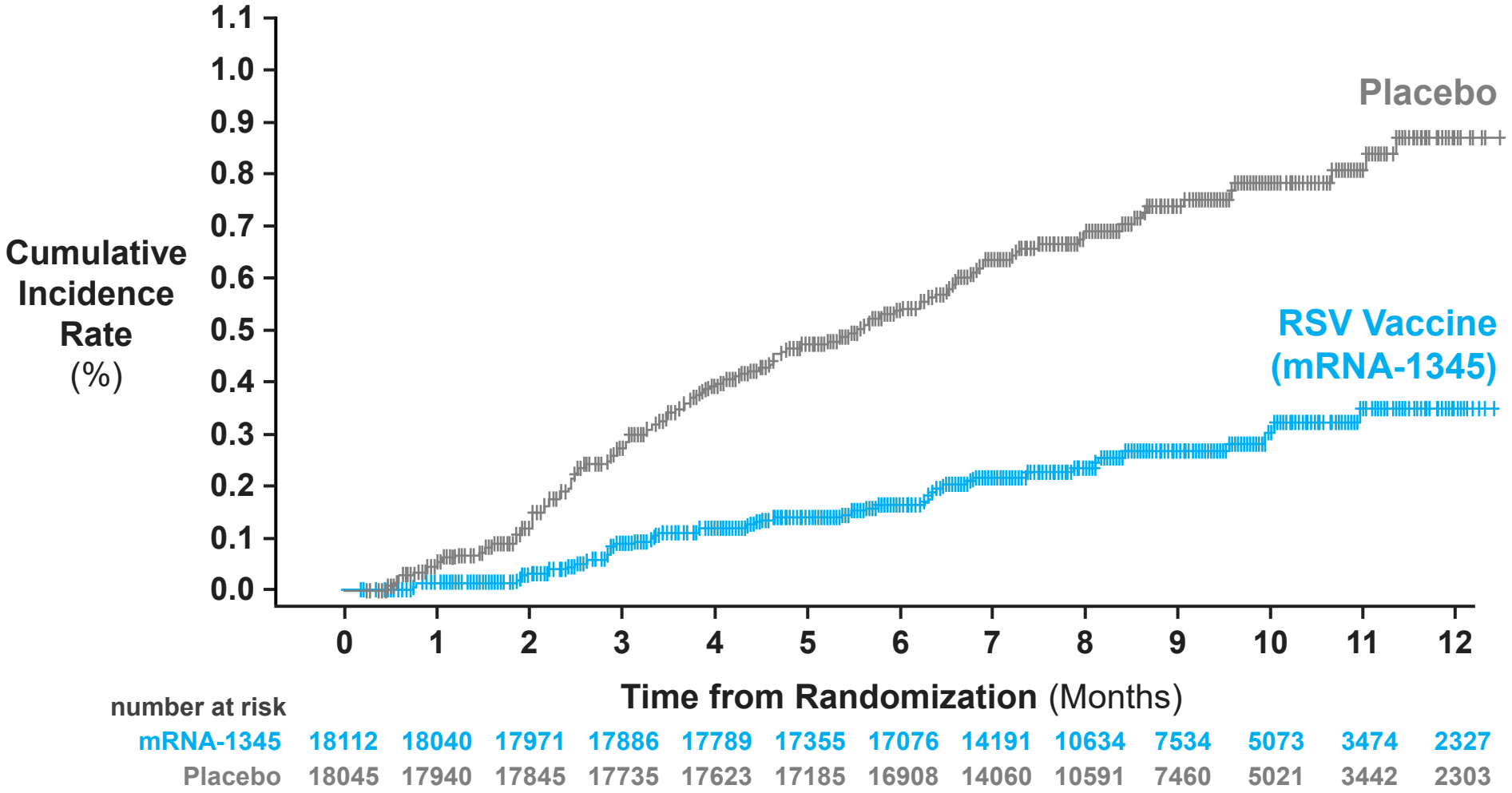
	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 18,112)	**Placebo** (N = 18,045)	**Vaccine Efficacy (%) Based on Hazard Ratios (95% CI)**
RSV LRTD ≥ 2 symptoms	47 (0.26%)	127 (0.70%)	**63.3%** (48.7%, 73.7%)
RSV LRTD ≥ 3 symptoms	19 (0.10%)	51 (0.28%)	**63.0%** (37.3%, 78.2%)
RSV ARD	86 (0.47%)	185 (1.03%)	**53.9%** (40.5%, 64.3%)

- Vaccine protection continues over a longer period (median 8.6 months) through high-transmission 2022/2023 RSV season
- Lower bound of the confidence interval continued to exceed 20%

Cumulative Incidence Curve – Efficacy Against RSV LRTD with ≥ 2 Symptoms among Adults ≥ 60 Years

Study 301 - Per-Protocol Efficacy Set

Additional Analysis



Vaccine Efficacy* (95% CI)

63.3% (48.7%, 73.7%)

- 8.6 months median follow-up (range 0.5-17.7 months)
- Separation in curves observed early and sustained through follow-up

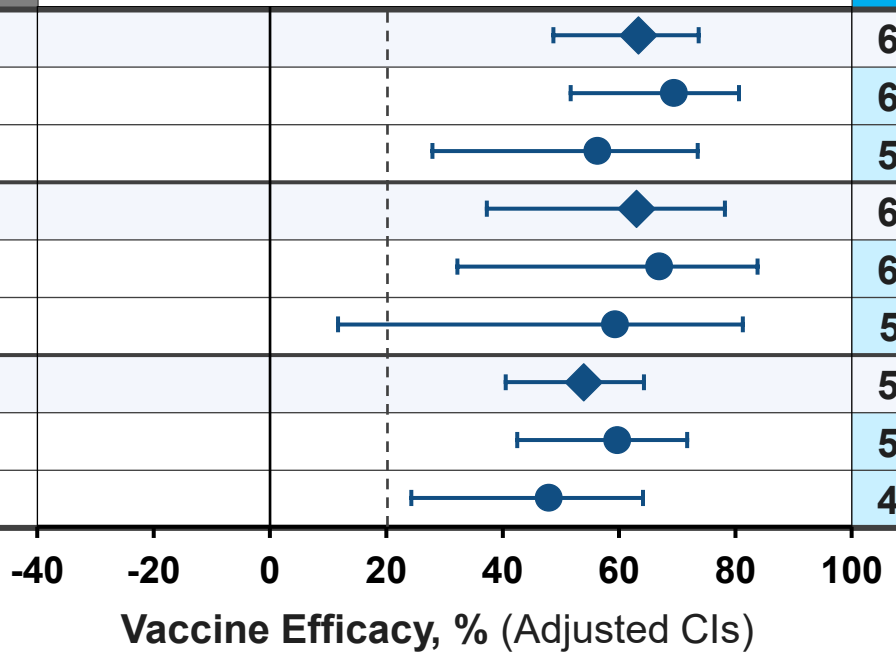
Data cutoff date: Apr 30, 2023; *based on hazard ratio

Vaccine Efficacy Against RSV-A and RSV-B by Endpoint

Study 301 - Per-Protocol Efficacy Set

Additional Analysis

		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)



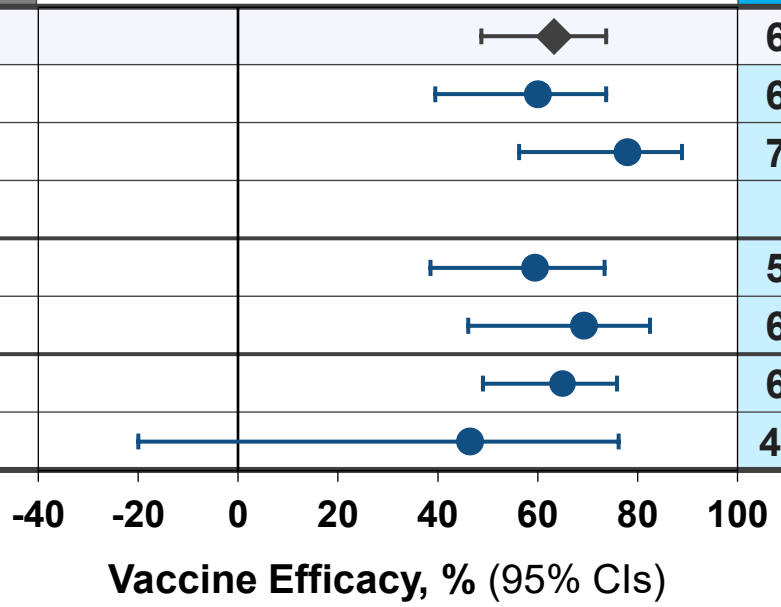
- Efficacy was observed for both RSV-A and RSV-B

Vaccine Efficacy by Age, Comorbidities, and Frailty Against RSV LRTD ≥ 2 Symptoms

Study 301 - Per-Protocol Efficacy Set

Additional Analysis

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	**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)



- Case splits favorable for mRNA-1345 with respect to age, comorbidities, and frailty
- Too few cases in ≥ 80-year-olds to assess efficacy

NE - nonestimable

Comorbidities include COPD, CHF, asthma, chronic respiratory disease, diabetes, advanced liver disease, advanced renal disease

Efficacy Against Severe LRTD and Hospitalizations Among Adults ≥ 60 Years

Study 301 - Post Hoc Analysis/Per Protocol Analysis

Additional Analysis

	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 18,112)	**Placebo** (N = 18,045)	**Vaccine Efficacy (%) Based on Hazard Ratios (95% CI)**
RSV-LRTD 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%** (-7.35, 86.45)
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:
  - Shortness of breath associated with RSV-LRTD
  - Medically attended RSV-LRTD (ER/urgent care visits)
- 2 hospitalizations in placebo recipients (both >70 years with comorbid conditions [asthma]; both recovered)

Based on April 30, 2023 cutoff
NE - nonestimable
1. Falsey et al *NEJM*, 2005; 2. Panozzo et al *ESWI*, 2023

Immunogenicity

Study 301

Immunogenicity Subset

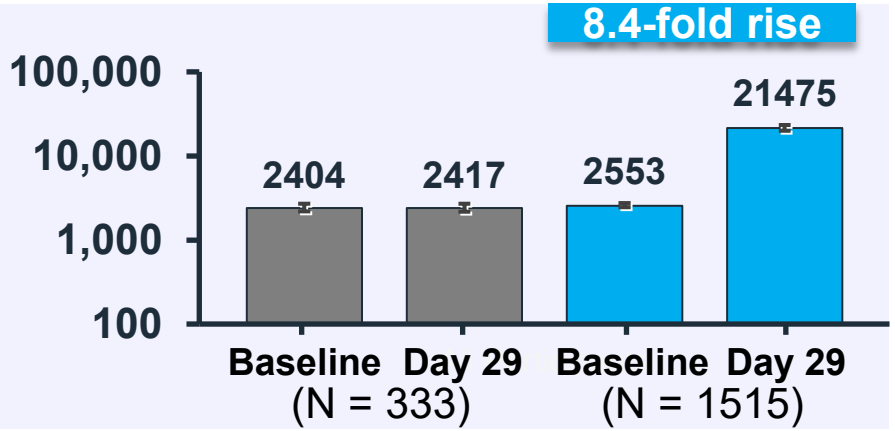
Neutralizing Antibody Response by RSV Subtype – Baseline and Day 29

Study 301 - Microneutralization Antibody (IU/mL)

Per Protocol Immunogenicity Set

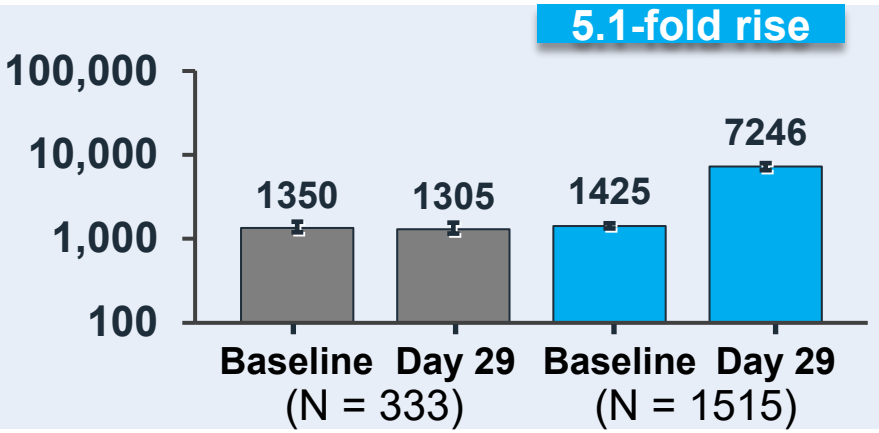
RSV-A Assay

GMT
IU/mL
(95% CI)



RSV-B Assay

GMT
IU/mL
(95% CI)



mRNA-1345 (50 µg)

Placebo

- Participants had baseline titers consistent with prior exposure to RSV
- One dose of 50 µg of mRNA-1345 increased titers by:
  - >8-fold for RSV-A
  - >5-fold for RSV-B

Neutralizing Antibody Response by RSV Subtype and Age – Baseline and Day 29

Study 301 – Microneutralization Antibody (IU/mL)

mRNA-1345 (50 µg)

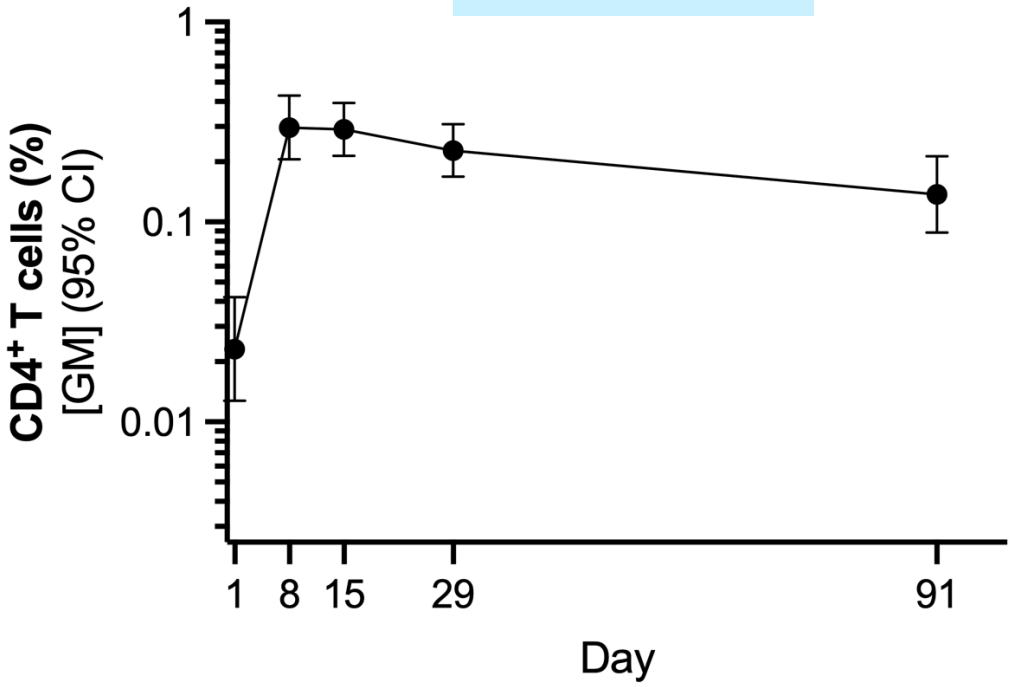
Per Protocol Immunogenicity Set

- Baseline titers similar across age groups
- Day 29 titers and fold rise are similar across age groups

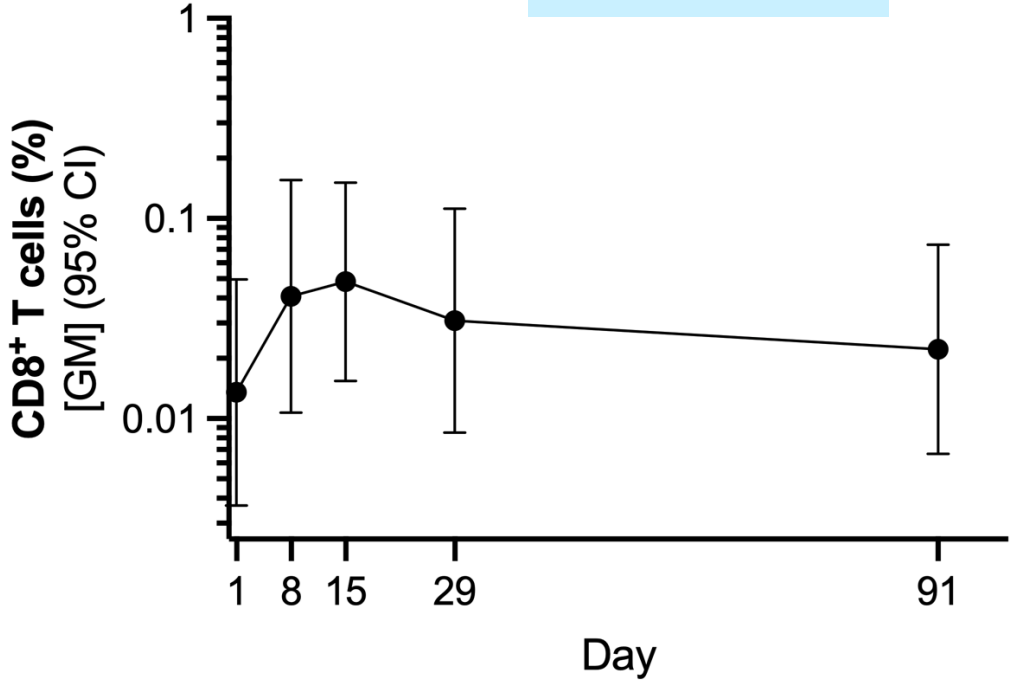
T-cell Responses Following Receipt of mRNA-1345

CRID-001 Study - 15 Adults, 50-75 Years Old

CD4+ T cells



CD8+ T cells

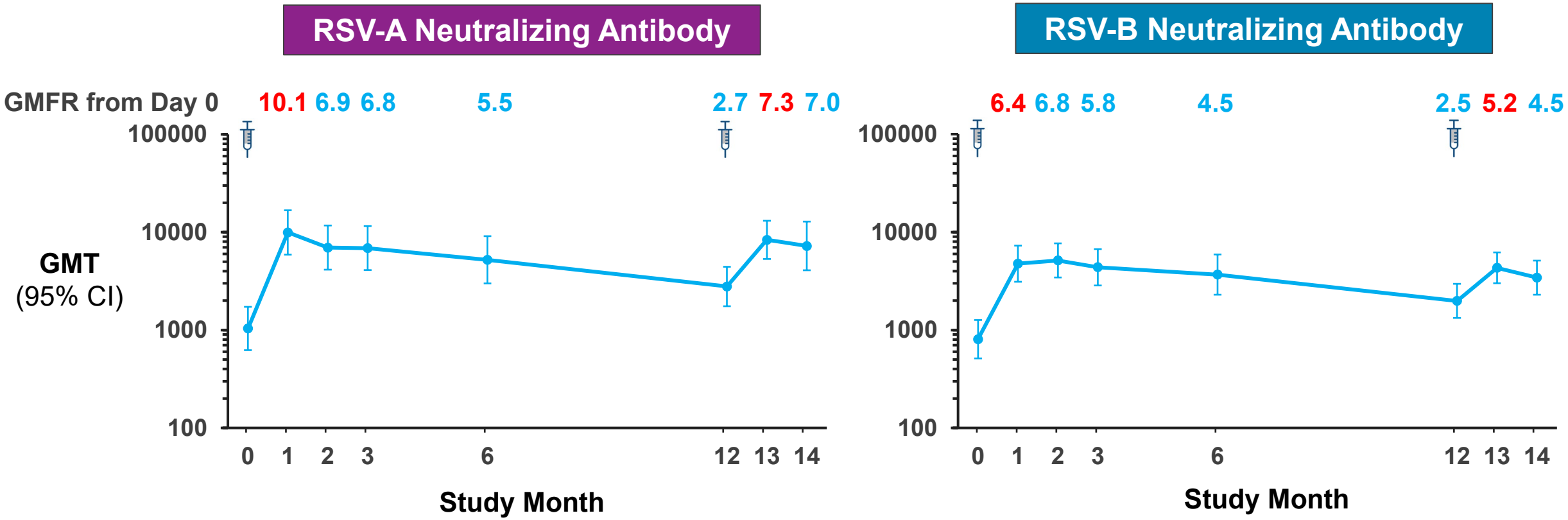


RSV-F antigen specific, Interferon-γ+ T-cells (intracellular cytokine staining assay)

- Vaccine elicits persistent CD4+ and CD8+ T-cell responses

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 detectable 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

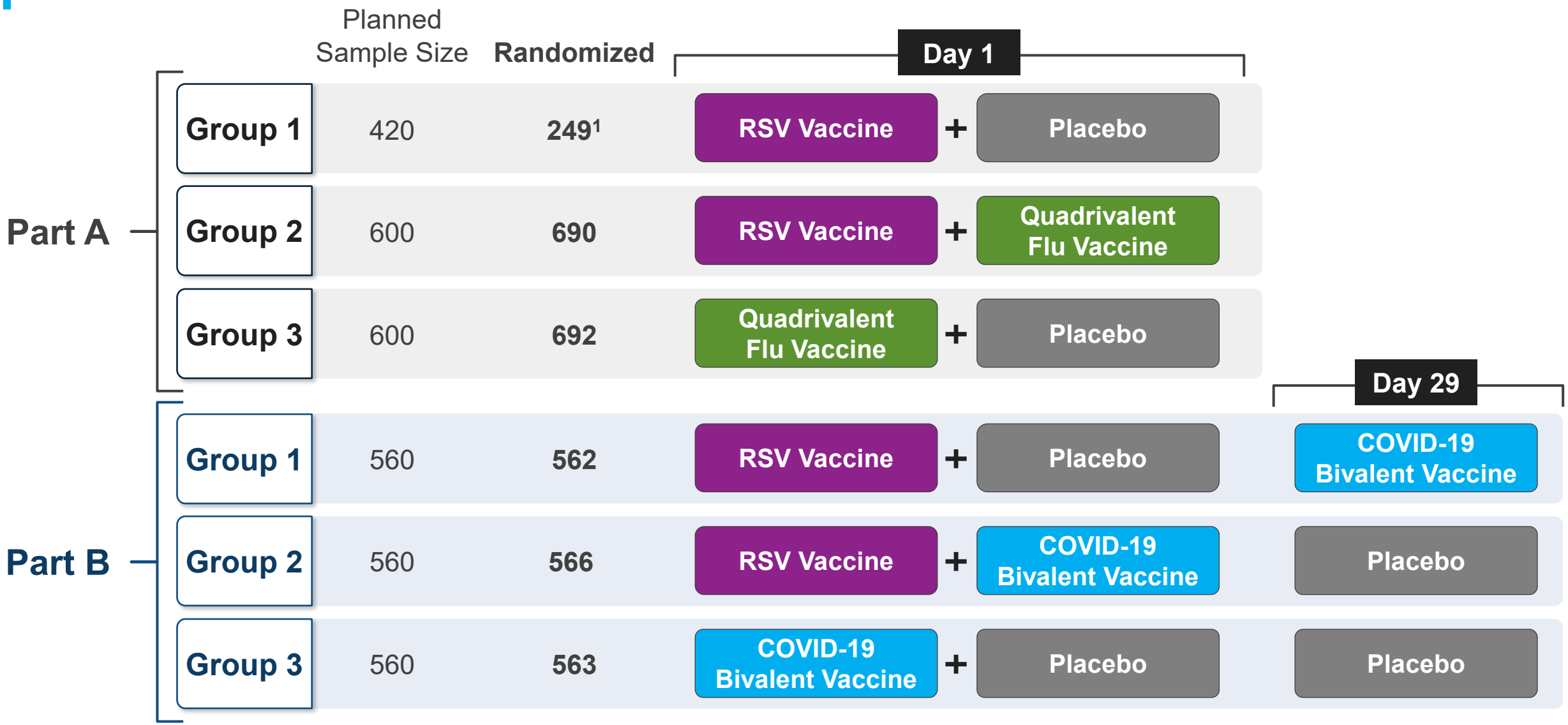
N = 14-18 adults

Simorellis et al, *ESWI* 2023

Concomitant Administration of RSV Vaccine (mRNA1345) with Quadrivalent Influenza Vaccine (Afluria) or Bivalent COVID-19 Vaccine (mRNA-1273.214)

Study 302, Parts A & B

Study 302: Safety and Immunogenicity Study of Concomitant Administration of mRNA-1345 with Quadrivalent Influenza Vaccine (Afluria) or COVID-19 Bivalent Vaccine in Adults ≥ 50

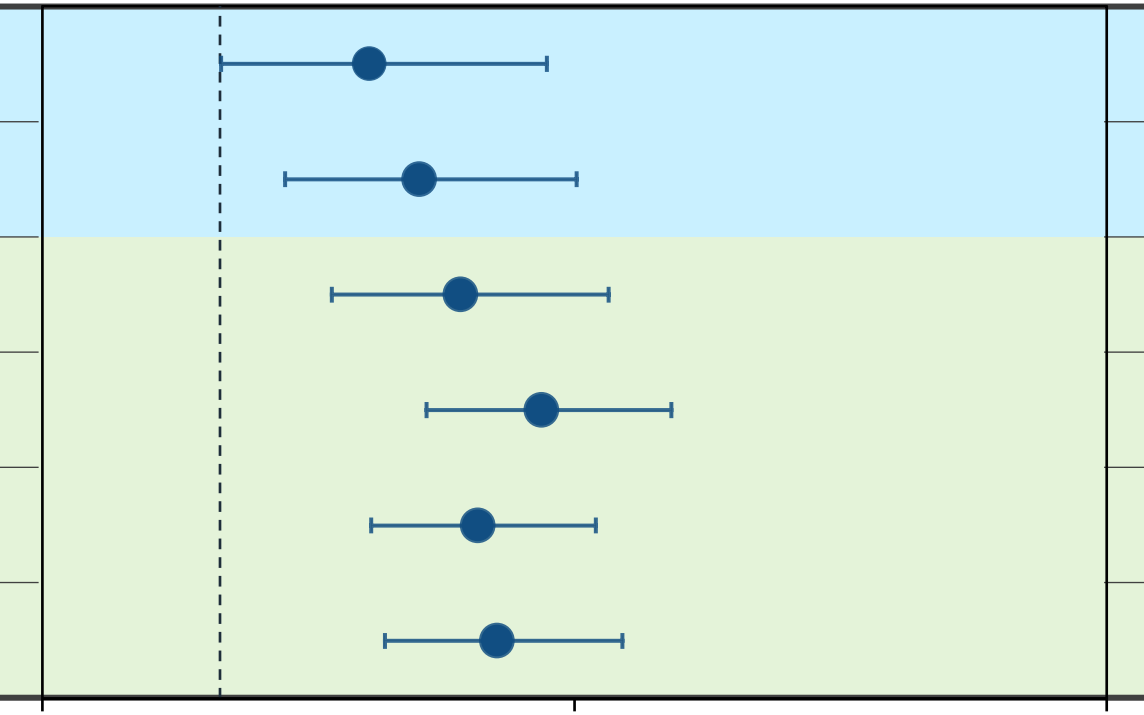


1. Due to randomization error, sample size lower than planned

Comparison of Day 29 Geometric Mean Titer Ratio (GMR) – Concomitant vs Nonconcomitant Administration of mRNA-1345 and Quadrivalent Influenza Vaccine

Study 302, Part A

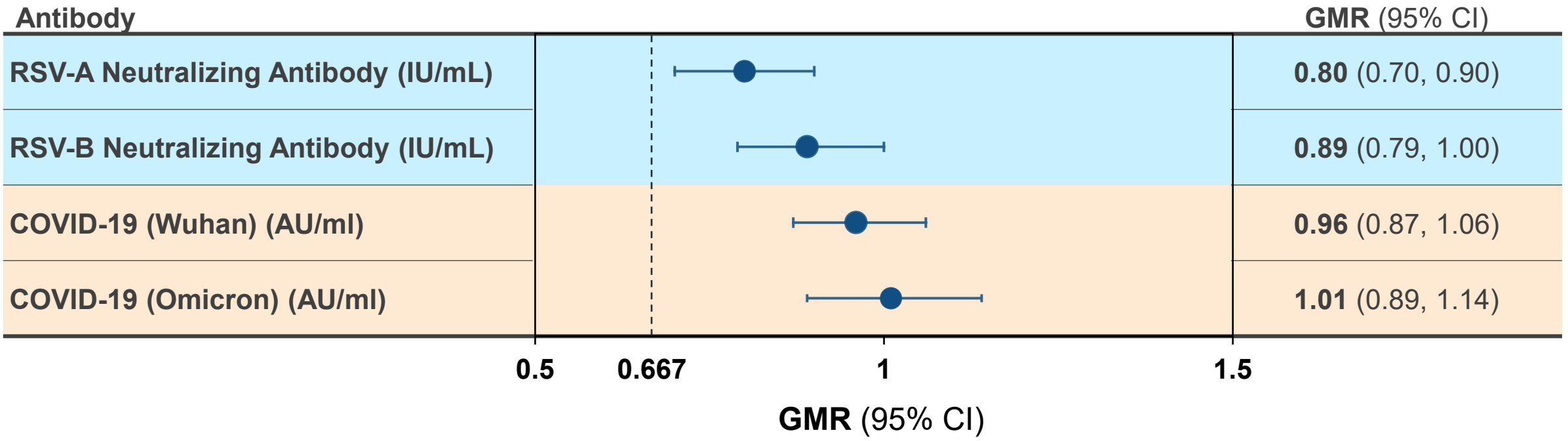
Antibody	**GMR** (95% CI)
RSV-A Neutralizing Antibody (IU/mL)	**0.81** (0.67, 0.97)
RSV-B Neutralizing Antibody (IU/mL)	**0.85** (0.73, 1.00)
Influenza A/H1N1 Antibody	**0.89** (0.77, 1.03)
Influenza A/H3N2 Antibody	**0.97** (0.86, 1.09)
Influenza B/Phuket Antibody	**0.91** (0.81, 1.02)
Influenza B/Washington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



All GMR non-inferiority criteria met (LB of the 2-sided 95% CI of GMR > 0.667)

Comparison of Day 29 Geometric Mean Titer Ratio (GMR) – Concomitant vs Nonconcomitant Administration of mRNA-1345 and COVID-19 Bivalent Vaccine

Study 302, Part B



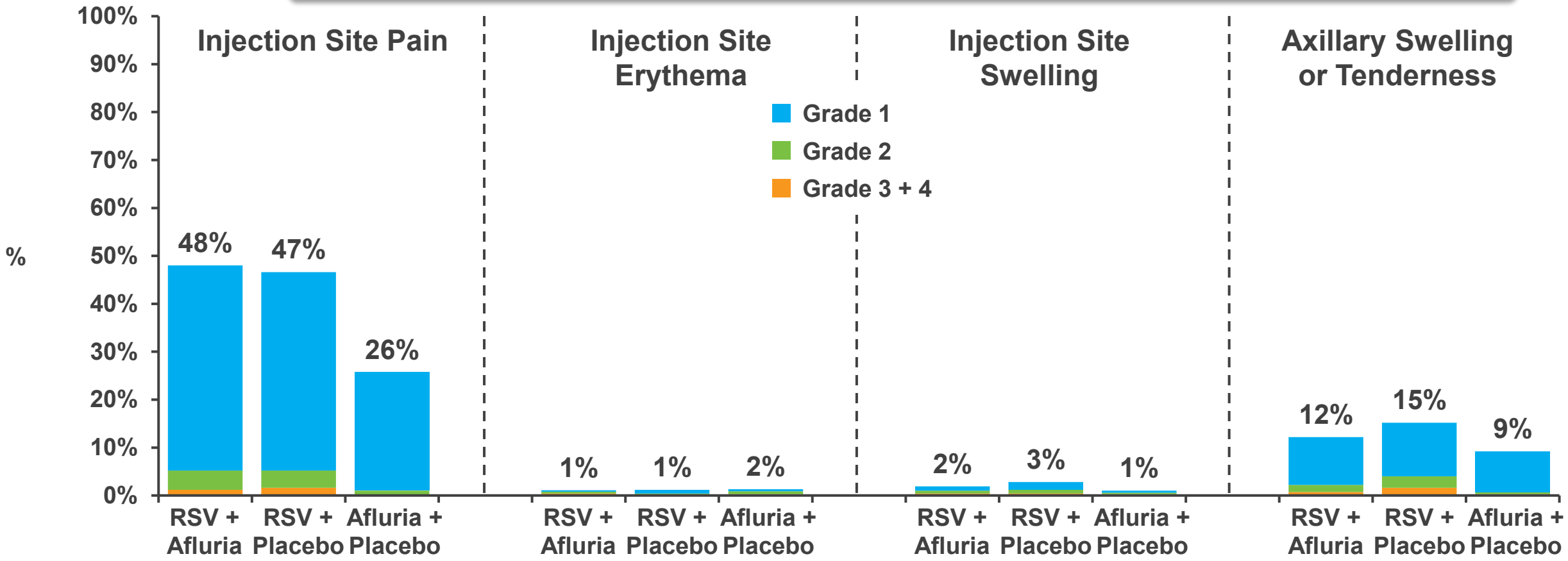
All GMR non-inferiority criteria met (LB of the 2-sided 95% CI of GMR > 0.667)

Solicited Local Reactions within 7 Days After mRNA-1345 Alone or Co-administered with Quadrivalent influenza Vaccine (Afluria) in Adults ≥ 50

Study 302, Part A - Solicited Safety Set

Solicited Safety Set

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



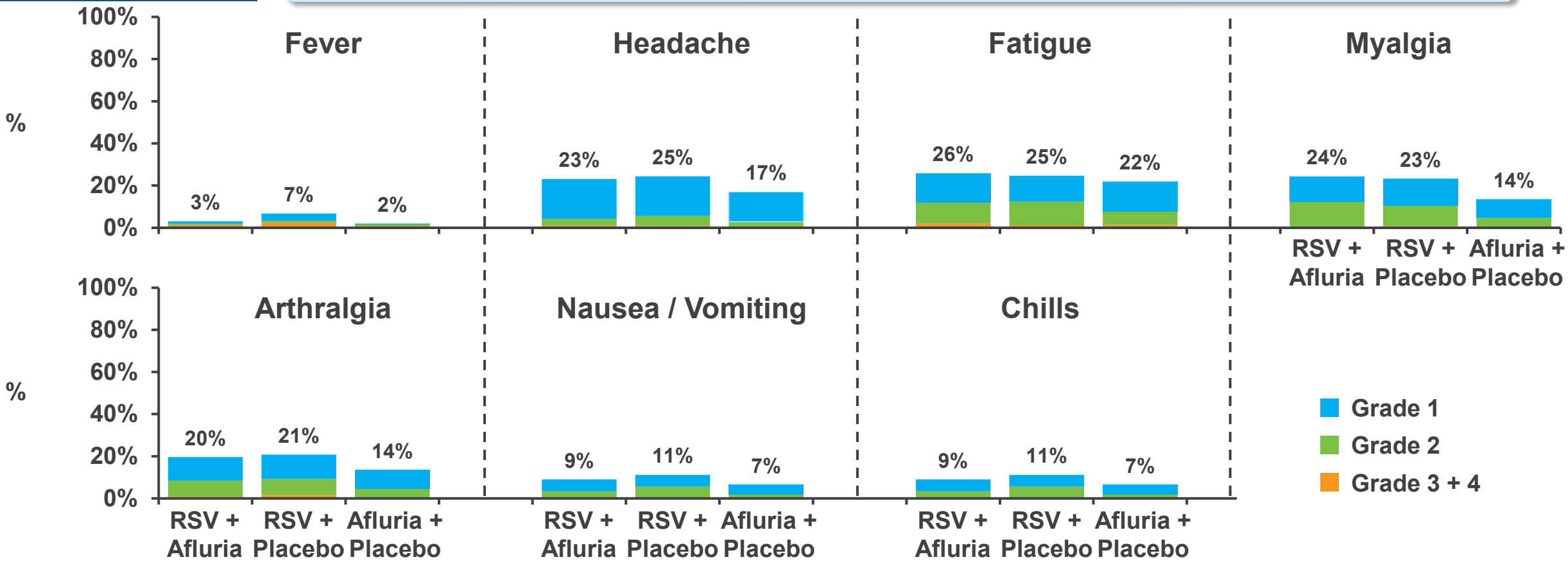
mRNA-1345 + Afluria, n= 678; mRNA-1345 + placebo, n= 249; Afluria + placebo; n= 683
One grade 4 event (0.4%) of axillary swelling or tenderness in mRNA-1345 + placebo group

Solicited Systemic Reactions within 7 Days After mRNA-1345 Alone or Co-administered with Quadrivalent Influenza Vaccine in Adults ≥ 50

Study 302, Part A - Solicited Safety Set

Solicited Safety Set

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



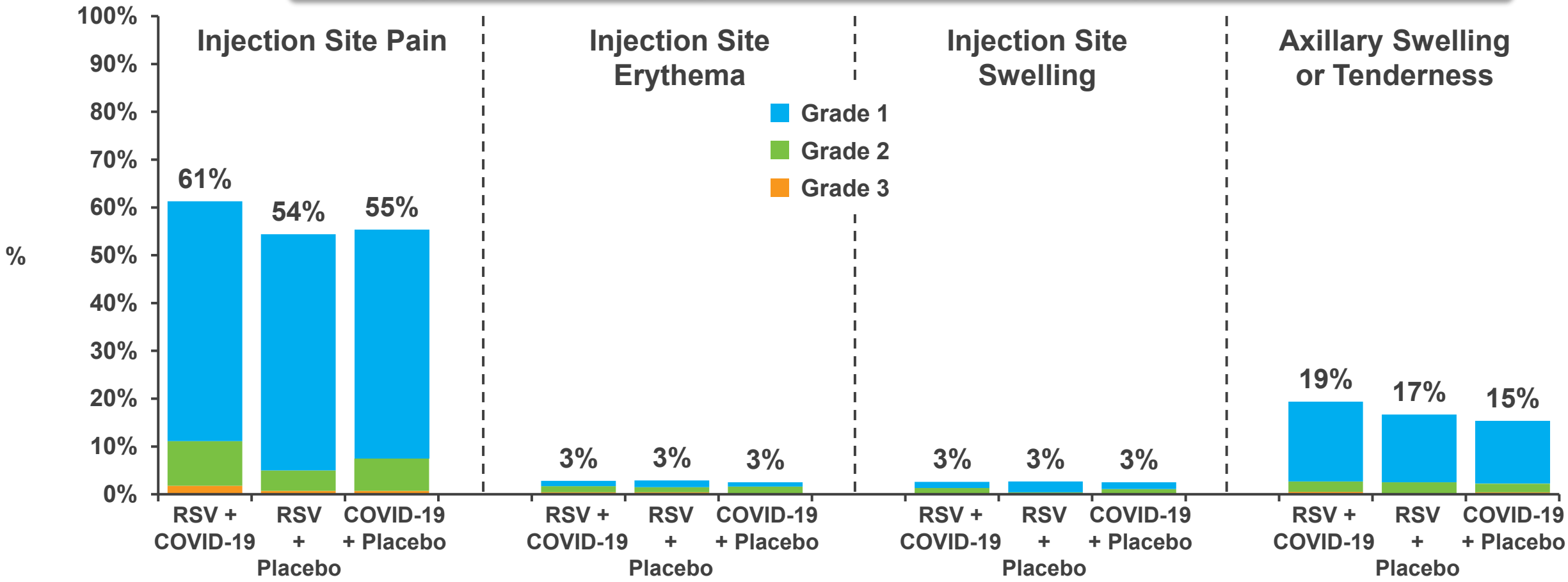
mRNA-1345 + Afluria, n= 678; mRNA-1345 + placebo, n= 249; Afluria + placebo; n= 683
Grade 4 fever reported in 1 recipient of mRNA 1345+ placebo

Solicited Local Reactions within 7 Days After mRNA-1345 Alone or Co-administered with COVID-19 Bivalent Vaccine in Adults ≥ 50

Study 302, Part B - Solicited Safety Set

Solicited Safety Set

Mostly grade 1, onset day 1-2, median duration of 2 days for RSV + COVID-19



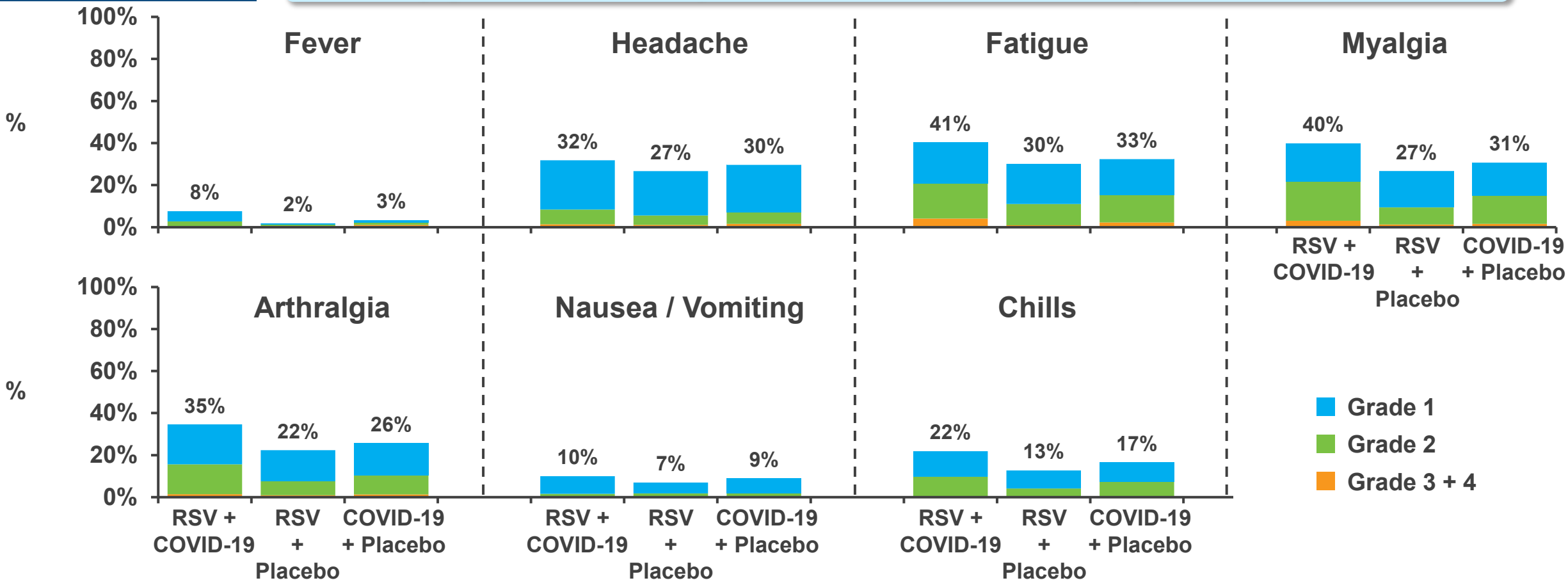
mRNA-1345 + COVID-19, n= 558; mRNA-1345 + placebo, n= 555; COVID-19 + placebo; n= 557
No grade 4 events

Solicited Systemic Reactions within 7 Days After mRNA-1345 Alone or Co-administered with COVID-19 Bivalent Vaccine in Adults ≥ 50

Study 302, Part B - Solicited Safety Set

Solicited Safety Set

Mostly grade 1, onset day 1-2, median duration of 2 days for RSV + COVID-19



mRNA-1345 + COVID-19 vaccine, n= 558; mRNA-1345 + placebo, n= 555; COVID-19 vaccine + placebo; n= 557
Grade 4 fever reported in 1 recipient of COVID-19 + placebo

Safety Events of Interest – Study of Concomitant Administration of mRNA-1345 with Influenza or COVID-19 Vaccine

Study 302 A and B – Based on 6 Months Follow-up

Safety Set

- No reports of:
  - Deaths, SAEs, or AESIs as assessed as related by the investigator
  - Anaphylaxis
  - Guillain Barre Syndrome
  - Acute disseminated encephalomyelitis (ADEM)
  - Bell's palsy/facial paralysis
  - Acute myocarditis or acute pericarditis

SUMMARY

Summary

Investigational RSV Vaccine (mRNA-1345)

Safety	▪ Vaccine generally well tolerated in >19,500 individuals ▪ No GBS, no ADEM, or other safety concerns
Efficacy	▪ Vaccine efficacious; met all regulatory criteria for licensure ▪ Continued to be efficacious through median 8.6 months follow-up ▪ Shown to prevent severe RSV disease (based on analysis of shortness of breath and medically attended RSV-LRTD)
Immunogenicity	▪ Strong humoral and cellular immune responses ▪ Detectable through 12 months post-vaccination; boosting observed with 1-year revaccination ▪ RSV-A & RSV-B nAb responses similar across age groups, including those ≥ 80 years old
Concomitant Administration	▪ Pre-specified immunogenicity criteria met & and no new safety signals observed with concomitant administration of mRNA-1345 with influenza vaccine or mRNA-COVID-19 vaccine

THANK YOU!

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