



Safety and Efficacy of mRNA-1345, an mRNA-based Vaccine Against Respiratory Syncytial Virus, in Adults 60 Years and Older

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February 23, 2023
Presented at the 7th ReSViNET Conference (RSVW 2023)
Lisbon, Portugal



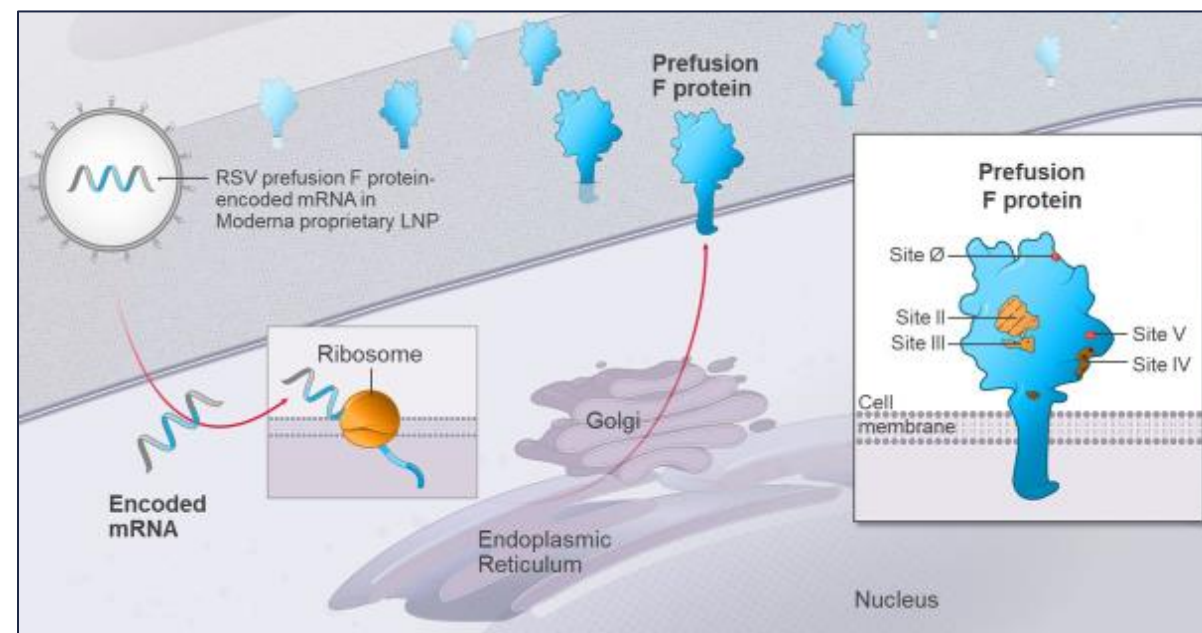
Disclosures, Acknowledgments, and Abstract Plain Language Summary

- EW, JG, SKS, RM, SM, AK, WH, LL, LEA, CAP, PG, AA, CAS, JM, and GLC are employees of Moderna, Inc., and hold stock/stock options in the company
- Medical writing and editorial assistance were provided by Jared Mackenzie, PhD, of MEDiSTRAVA in accordance with Good Publication Practice (GPP3) guidelines, funded by Moderna, Inc., and under the direction of the authors
- This study was funded by Moderna, Inc.
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mRNA-1345, an mRNA-based RSV Vaccine, Encodes for a Stabilized Prefusion F Glycoprotein

- **mRNA-1345** is an mRNA-based RSV vaccine candidate consisting of a single mRNA sequence encoding the membrane-anchored RSV F glycoprotein stabilized in the prefusion conformation
 - Prefusion F elicits superior neutralizing antibody responses compared to post-fusion F^{1,2}
 - F protein antibodies cross-react between RSV-A and RSV-B³
 - Phase 1 data show that mRNA-1345 is well tolerated and boosts antibody levels through 6 months⁴



F, fusion; LNP, lipid nanoparticle; mRNA, messenger ribonucleic acid.

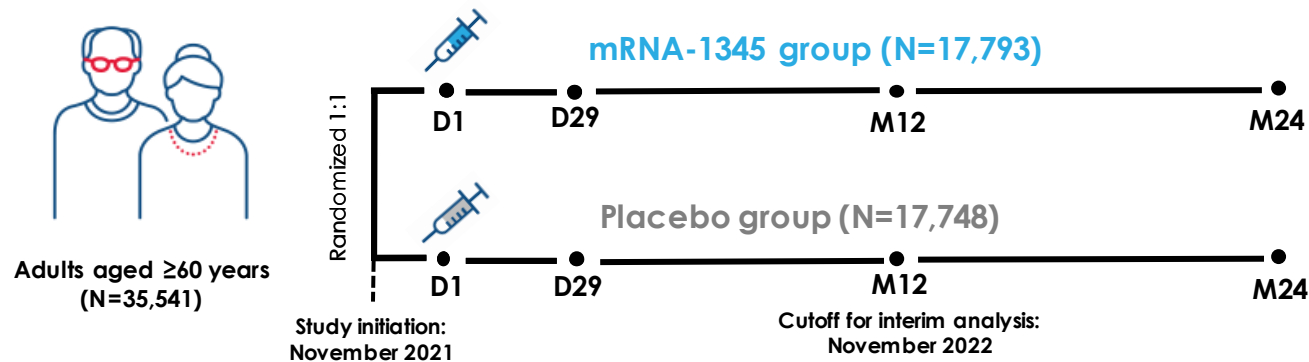
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mRNA-1345 Phase 2/3 Clinical Trial

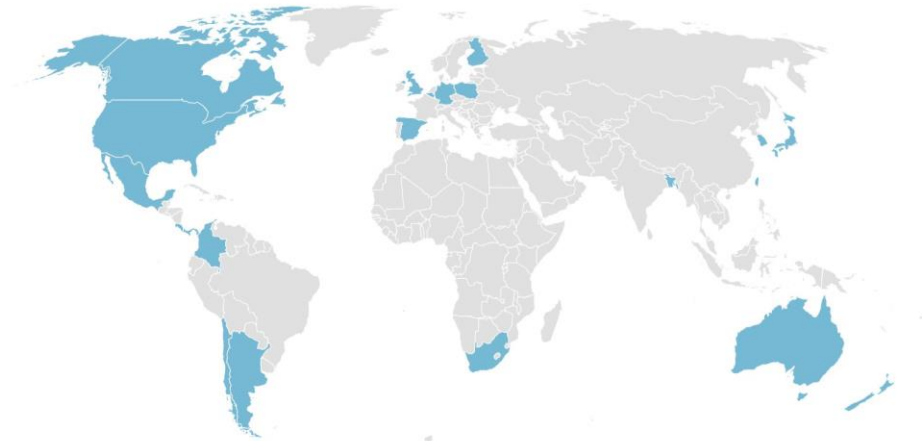


- In this ongoing phase 2/3, randomized, double-blind, placebo-controlled, case-driven study in adults aged ≥ 60 years (NCT05127434)¹, 35,541 participants from 22 countries were randomized 1:1 to receive 1 dose of mRNA-1345 50 μ g or placebo
 - Healthy participants were included, as well as medically stable participants with ≥ 1 chronic medical diagnoses

Study Schedule – Phase 3



Trial Sites



Primary Efficacy Endpoints

- Vaccine efficacy of mRNA-1345 to **prevent a first episode of RSV lower respiratory tract disease (LRTD) with ≥ 2 or ≥ 3 symptoms** between 14 days to 12 months following injection

Note: Study schedule data are from the Randomization Set analysis population.

Solicited local and systemic adverse reactions were collected up to 7 days post-injection; unsolicited adverse events were collected up to 28 days post-injection; medically-attended adverse events, adverse events of special interest, serious adverse events, and adverse events leading to withdrawal are collected up to 24 months post-injection.

D, day; LRTD, lower respiratory tract disease; M, month; mRNA, messenger ribonucleic acid; RSV, respiratory syncytial virus.

¹ClinicalTrials.gov. NCT05127434. Accessed January 31, 2023. <https://clinicaltrials.gov/ct2/show/NCT05127434>

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mRNA-1345 Phase 2/3 Clinical Trial: Efficacy Endpoint Definition

Two Primary Endpoint Definitions for RSV Lower Respiratory Tract Disease (LRTD)

RSV LRTD with 2 or more lower respiratory symptoms

- RT-PCR-confirmed RSV *PLUS*
- Radiologic evidence of pneumonia
OR
- New or worsening of 2 or more of the following symptoms for ≥ 24 hours:

RSV LRTD with 3 or more lower respiratory symptoms

- RT-PCR-confirmed RSV *PLUS*
- Radiologic evidence of pneumonia
OR
- New or worsening of 3 or more of the following symptoms for ≥ 24 hours:

LRTD Symptoms

- Shortness of breath
- Cough and/or fever
- Wheezing/rales/rhonchi
- Sputum production
- Tachypnea
- Hypoxemia
- Pleuritic chest pain



Demographics and Baseline Characteristics

	mRNA-1345 (N=17,793)	Placebo (N=17,748)
Age at Enrollment (Years), Mean (SD)	68.1 (6.19)	68.1 (6.20)
Age Group, n (%)^a		
60 to 69 Years	11,315 (63.6)	11,270 (63.5)
70 to 79 Years	5493 (30.9)	5478 (30.9)
≥80 Years	985 (5.5)	1000 (5.6)
Sex, n (%)		
Male	9100 (51.1)	9004 (50.7)
Female	8693 (48.9)	8744 (49.3)
Comorbidities of Interest, n (%)^b		
0	12,535 (70.4)	12,593 (71.0)
≥1	5258 (29.6)	5155 (29.0)

	mRNA-1345 (N=17,793)	Placebo (N=17,748)
Race Groups, n (%)		
White	11,285 (63.4)	11,254 (63.4)
Black	2210 (12.4)	2173 (12.2)
Asian	1541 (8.7)	1535 (8.6)
Other ^c	2688 (15.1)	2680 (15.1)
Unknown/Not Reported	69 (0.4)	106 (0.6)
Ethnicity, n (%)		
Hispanic or Latino	6112 (34.4)	6162 (34.7)
Not Hispanic or Latino	11,495 (64.6)	11,377 (64.1)
Unknown	27 (0.2)	22 (0.1)
Not Reported	159 (0.9)	187 (1.1)

- Demographics and baseline characteristics were well matched across groups

Note: Data are from the Randomization Set analysis population.

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; LRTD, lower respiratory tract disease; mRNA, messenger ribonucleic acid; SD, standard deviation.

^aDerived from age and risk collected on electronic case report forms. ^bComorbidities of interest include COPD, asthma, chronic respiratory disease, diabetes, CHF, advanced liver disease, or advanced renal disease. ^cOther race includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, Other, or Multiple.

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Overview of Solicited Adverse Reactions

	mRNA-1345	Placebo
Solicited local adverse reactions within 7 days		
Solicited local adverse reactions within 7 days, n/N (%)	10,367/17,662 (58.7%)	2845/17,593 (16.2%)
Grade 3 or greater cases, n/N (%)	558/17,662 (3.2%)	305/17,593 (1.7%)
Solicited systemic adverse reactions within 7 days		
Solicited systemic adverse reactions within 7 days, n/N (%)	8432/17,662 (47.7%)	5798/17,597 (32.9%)
Grade 3 or greater cases, n/N (%)	710/17,662 (4.0%)	508/17,597 (2.9%)

- To date, most solicited adverse reactions were mild to moderate
- The most commonly reported solicited adverse reactions in the mRNA-1345 group were injection site pain, fatigue, headache, myalgia, and arthralgia

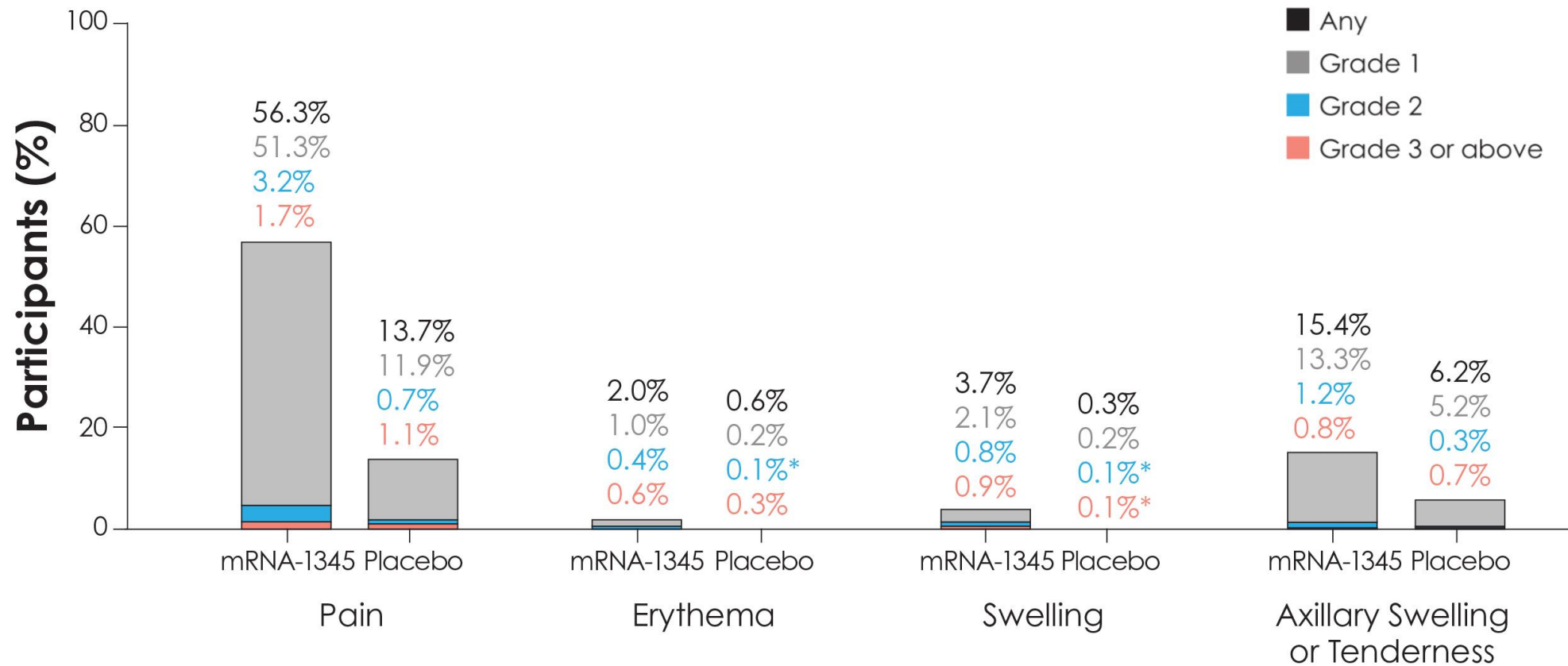
Note: Data are from the Solicited Safety Set analysis population.

mRNA, messenger ribonucleic acid.

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Percentage of Participants With Solicited Local Adverse Reactions Within 7 Days



- Pain at the injection site (mostly grade 1) was the most frequently reported local adverse reaction

Note: Data are from the Solicited Safety Set analysis population.

Summary of participants with solicited adverse reactions within 7 days after injection by grade; placebo (n = 17,598); mRNA-1345 50 µg (n = 17,665).

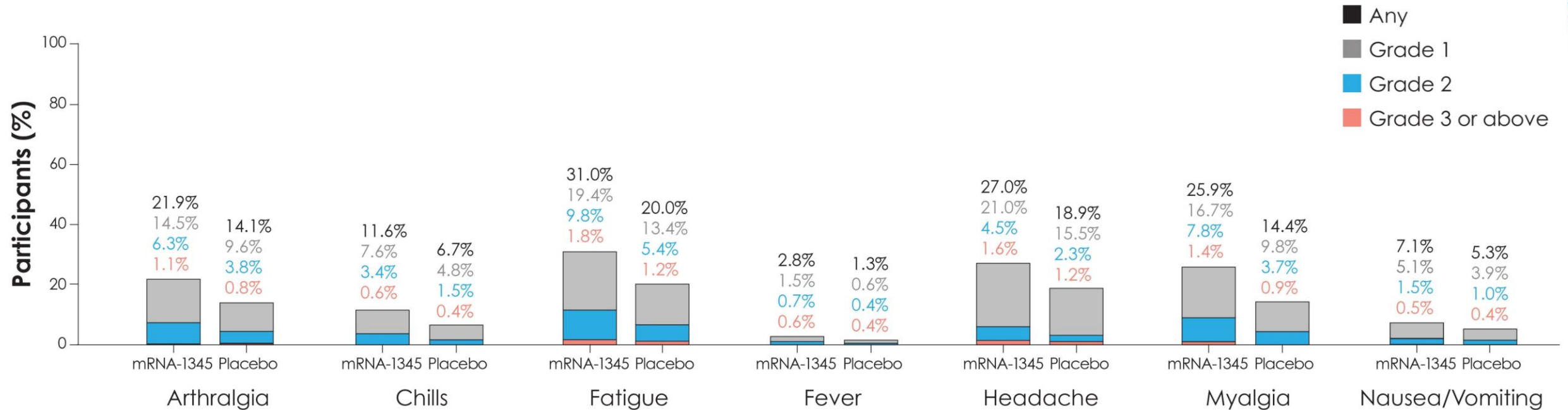
Note: *For placebo, grade 2 for erythema and grade 2 and grade 3 or above for swelling are <0.1%.

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Percentage of Participants With Solicited Systemic Adverse Reactions Within 7 Days



- Arthralgia, fatigue, headache, and myalgia were the most frequently reported systemic adverse reactions

Note: Data are from the Solicited Safety Set analysis population.

Summary of participants with solicited adverse reactions within 7 days after injection by grade; placebo (n = 17,598); mRNA-1345 50 µg (n = 17,665).

mRNA, messenger ribonucleic acid.

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Efficacy of mRNA-1345 Against RSV LRTD

	mRNA-1345 (N=17,572)	Placebo (N=17,516)
RSV LRTD with ≥2 symptoms		
Cases, n/N (%) ^{a,b}	9/17,572 (0.05%)	55/17,516 (0.31%)
VE (%) based on hazard ratios (alpha adjusted 95.88% CI) ^c	83.7% (66.0%, 92.2%)	
RSV LRTD with ≥3 symptoms		
Cases, n/N (%) ^{a,b}	3/17,572 (0.02%)	17/17,516 (0.10%)
VE (%) based on hazard ratios (alpha adjusted 96.36% CI) ^c	82.4% (34.8%, 95.3%)	

Note: Data are from the Per-Protocol Efficacy Set analysis population, 14 days to 12 months post-injection.

CI, confidence interval; LRTD, lower respiratory tract disease; mRNA, messenger ribonucleic acid; RT-PCR, reverse transcription polymerase chain reaction; VE, vaccine efficacy.

^aProtocol-defined RSV-LRTD with ≥2 and ≥3 symptoms is based on eligible symptoms onset within a timeframe of +/- 14 days from positive RSV RT-PCR collection date.

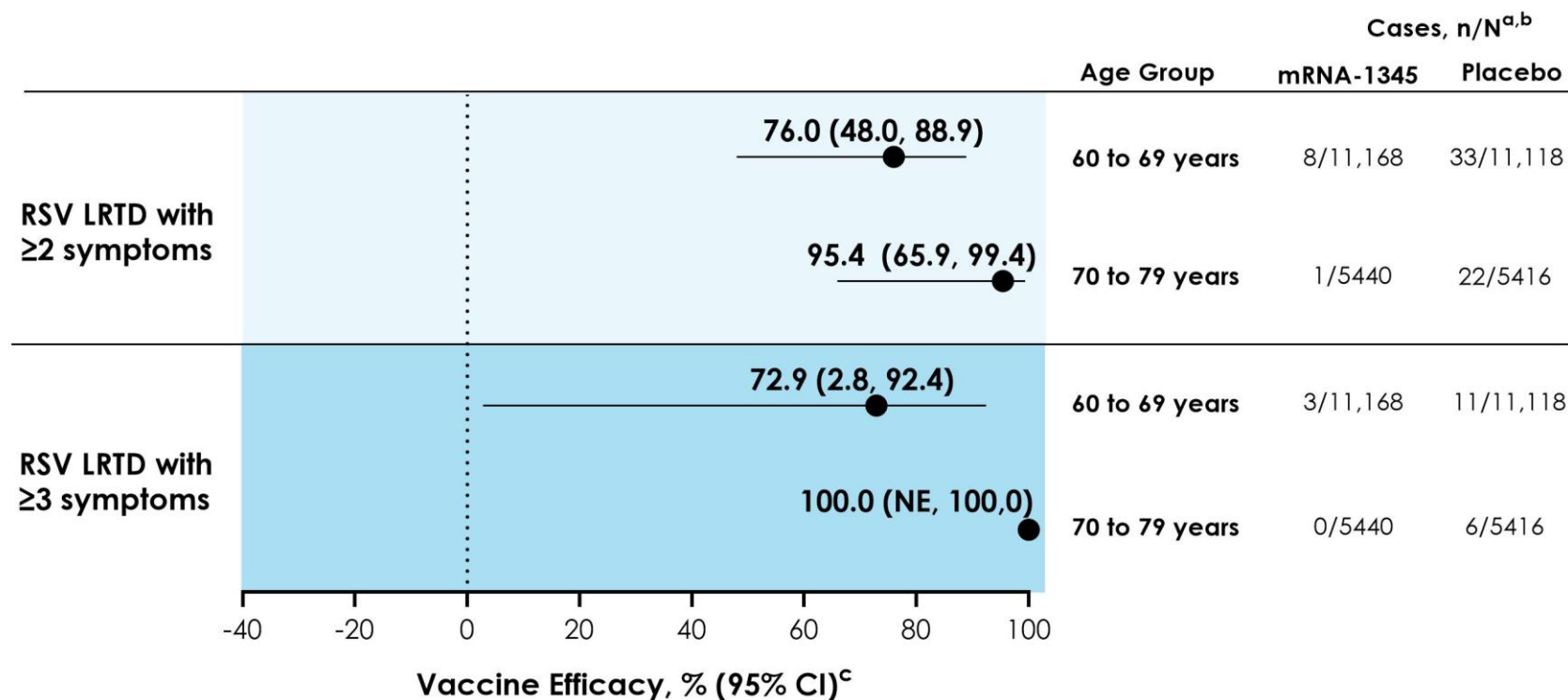
^bThe time to first occurrence of protocol-defined RSV-LRTD with ≥2 and ≥3 symptoms will be calculated as date of case — date of randomization + 1.

^cVE is defined as 100% x (1 — hazard ratio [mRNA-1345 vs. placebo]). The CI for VE is based on a stratified Cox proportional hazard model with Efron's method of tie handling and with the treatment group as a fixed effect, adjusting for stratification factors at randomization.

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Efficacy of mRNA-1345 Against RSV LRTD Across Age Groups



- In adults ≥80 years, no cases of RSV LRTD with ≥2 or ≥3 symptoms were observed (mRNA-1345, n/N=0/964; PBO, n/N=0/982)

Note: Data are from the Per-Protocol Efficacy Set analysis population, 14 days to 12 months post-injection.

CI, confidence interval; LRTD, lower respiratory tract disease; mRNA, messenger ribonucleic acid; NE, not evaluated; PBO, placebo; RSV, respiratory syncytial virus; RT-PCR, reverse transcription polymerase chain reaction; VE, vaccine efficacy

^aProtocol-defined RSV-LRTD with ≥2 and ≥3 symptoms is based on eligible symptoms onset within a timeframe of +/- 14 days from positive RSV RT-PCR collection date.

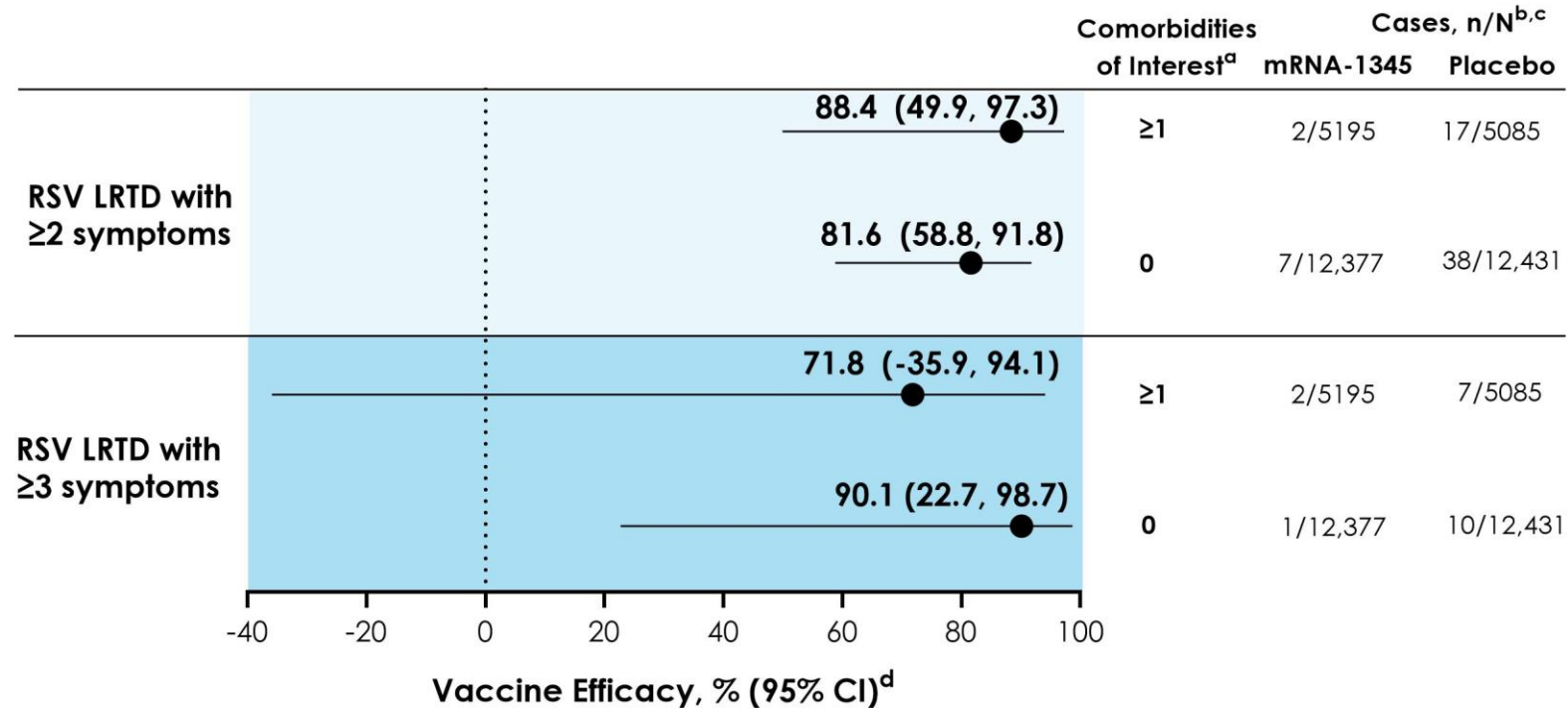
^bThe time to first occurrence of protocol-defined RSV-LRTD with ≥2 and ≥3 symptoms will be calculated as date of case — date of randomization + 1.

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Efficacy of mRNA-1345 Against RSV LRTD in Participants With Pre-existing Comorbidities



Note: Data are from the Per-Protocol Efficacy Set analysis population, 14 days to 12 months post-injection.

CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; LRTD, lower respiratory tract disease; mRNA, messenger ribonucleic acid; RSV, respiratory syncytial virus; RT-PCR, reverse transcription polymerase chain reaction; VE, vaccine efficacy.

^aComorbidities of interest include COPD, asthma, chronic respiratory disease, diabetes, CHF, advanced liver disease, or advanced renal disease. ^bProtocol-defined RSV-LRTD with ≥2 and ≥3 symptoms is based on eligible symptoms onset within a timeframe of +/- 14 days from positive RSV RT-PCR collection date. ^cThe time to first occurrence of protocol-defined RSV-LRTD with ≥2 or ≥3 symptoms will be calculated as date of case — date of randomization + 1. ^dVE is defined as 100% x (1 — hazard ratio [mRNA-1345 vs. placebo]). The CI for VE is based on a stratified Cox proportional hazard model with Efron's method of tie handling and with the treatment group as a fixed effect, adjusting for stratification factors at randomization.

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Conclusions

- mRNA-1345 was well tolerated and had an acceptable safety profile; solicited adverse reactions were mostly grade 1 or grade 2 in severity
- A single dose of mRNA-1345 50 µg is efficacious in preventing RSV LRTD with ≥ 2 or ≥ 3 symptoms in adults aged ≥ 60 years within 14 days to 12 months following injection
- Vaccine efficacy was consistently high across all age groups and in participants with pre-existing comorbidities
- The phase 3 clinical trial of mRNA-1345 in adults aged ≥ 60 years is ongoing, with additional supportive analyses planned through 24 months

LRTD, lower respiratory disease; mRNA, messenger ribonucleic acid; RSV, respiratory syncytial virus.

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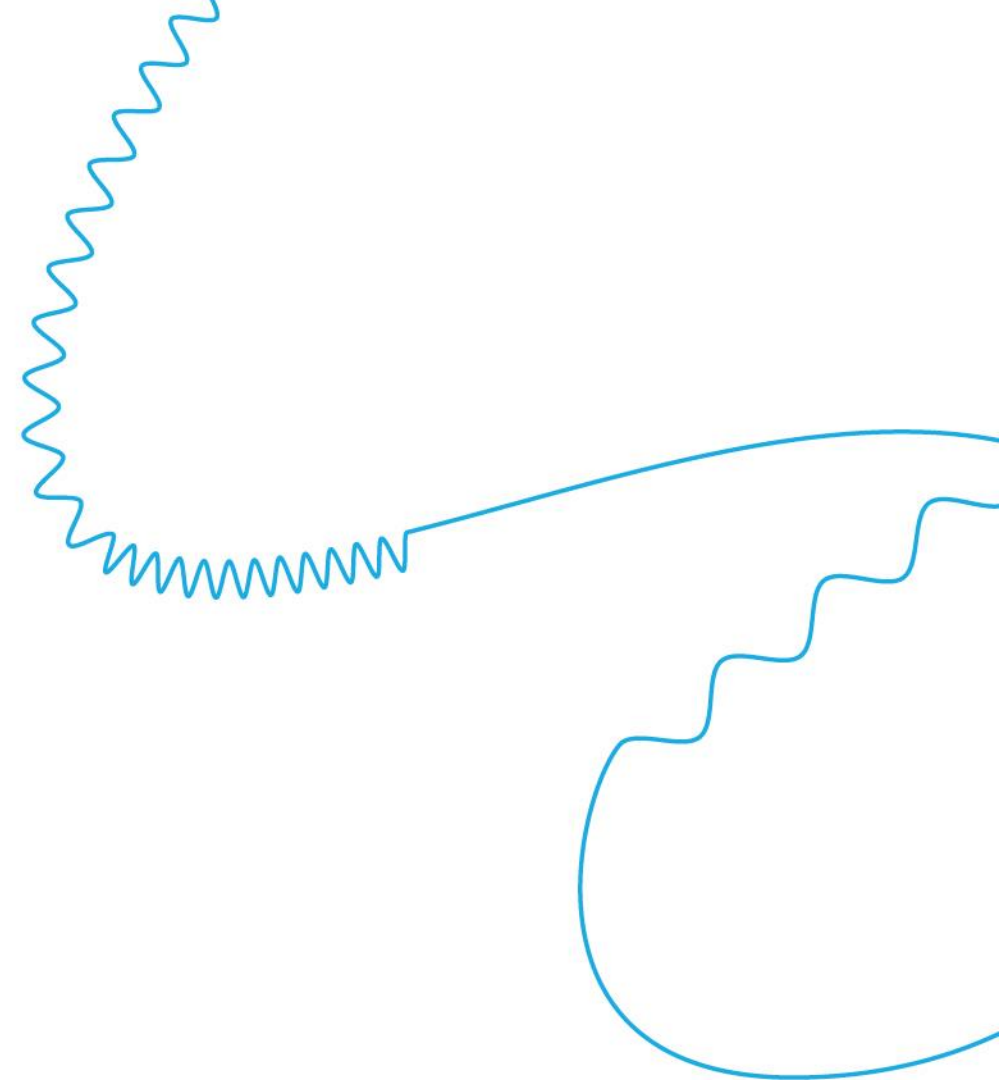
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RSV, respiratory syncytial virus.

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