mRNA-1010, an mRNA-Based Influenza Vaccine, Is Safe and Efficacious in Adults Aged ≥50 Years

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Disclosures and Acknowledgments

- Elissa Malkin, Evelyn Du, Agi Buchanan, Bryony Hicks, and Eleanor Wilson are employees of Moderna, Inc., and hold stock/stock options in the company
- Anita Kohli is an employee of The Institute for Liver Health Arizona and has no conflicts of interest to disclose
- Rebecca Clark is an employee of Layton Medical Centre - General Practice and has no conflicts of interest to disclose
- Isabel Leroux-Roels is an employee of Ghent University and Ghent University Hospital and received funding for the conduct of vaccine trials from Moderna, GSK, Icosavax, Virometix, Janssen Vaccines, Osivax, MSD, Astrivax, Sumitomo Pharma, and CSL Seqirus; and for consulting services (paid to her institution) from Janssen Vaccines, CSL Seqirus and MSD
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Malkin E, Kohli A, Clark R, et al. mRNA-1010, an mRNA-Based Influenza Vaccine, Is Safe and Efficacious in Adults Aged ≥50 Years. Presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA..

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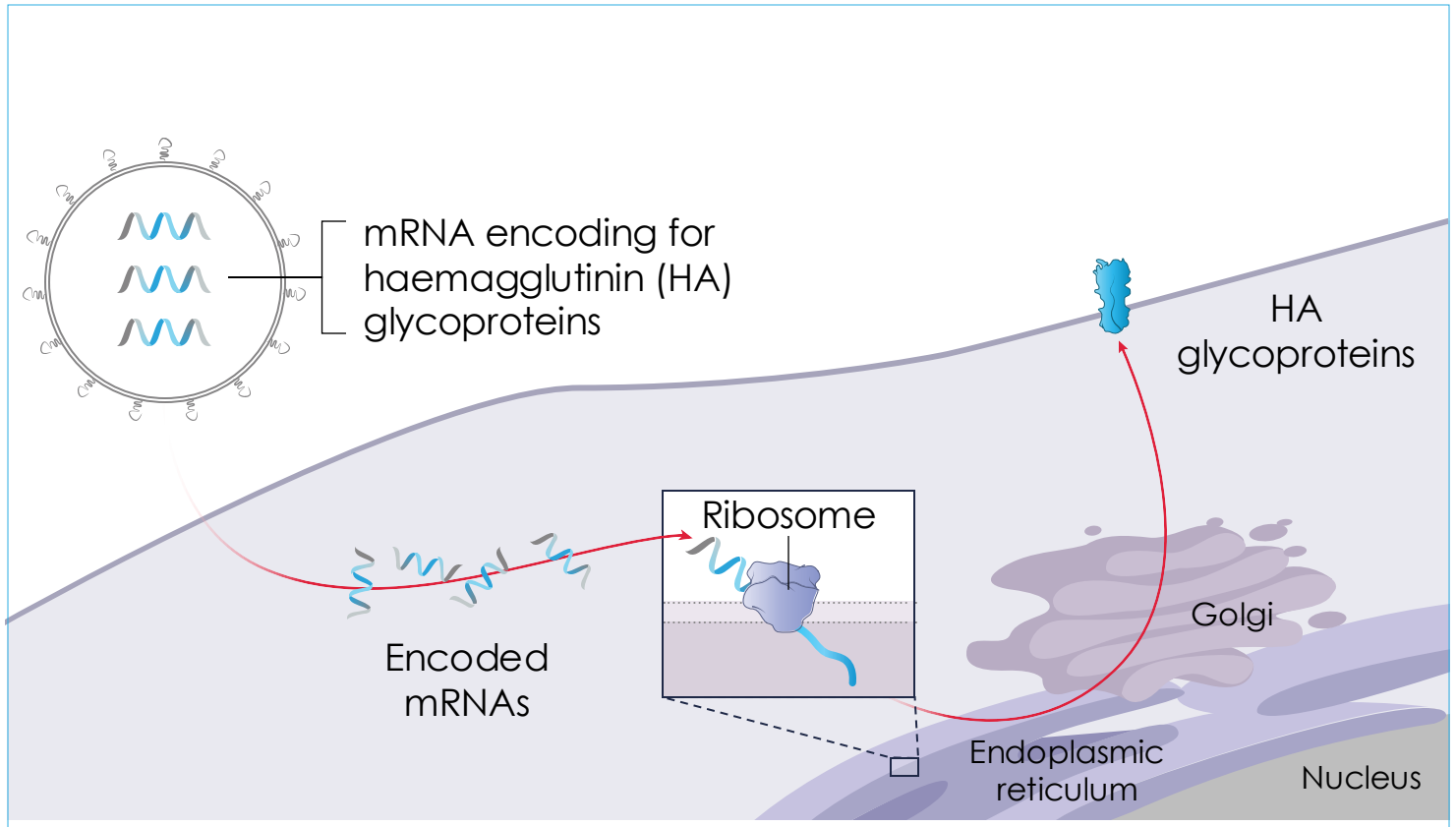
mRNA-1010: An mRNA-Based Seasonal Influenza Vaccine Candidate

- **Potential to address several limitations associated with currently licensed influenza vaccines**[1-4]
  - Encodes specific antigen protein (precise match)
  - No requirement for egg-based or other complex culture systems
  - Reduced production time allowing for strain selection closer to start of influenza season and decreasing risk for mismatch
- **Elicits superior immunogenicity compared to licensed standard dose (in adults aged 18-64 years) and high dose (in adults aged ≥65 years) licensed influenza vaccine comparators**[5]



mRNA-1010 encodes membrane-bound HA of WHO-recommended seasonal influenza strains

HA, haemagglutinin; WHO, World Health Organization.

1. World Health Organization. *Wkly Epidemiol Rec*. 2022;19:185–208. 2. Barr IG, et al. *NPJ Vaccines*. 2018; 3:44. 3. Dolgin E. *Nat Rev Drug Discov*. 2021; 20:801-803. 4.Okoli GN, et al. *Vaccine*. 2021; 39:1225-1240. 5. Soens M, et al. *Vaccine*. 2025; 50:126874.

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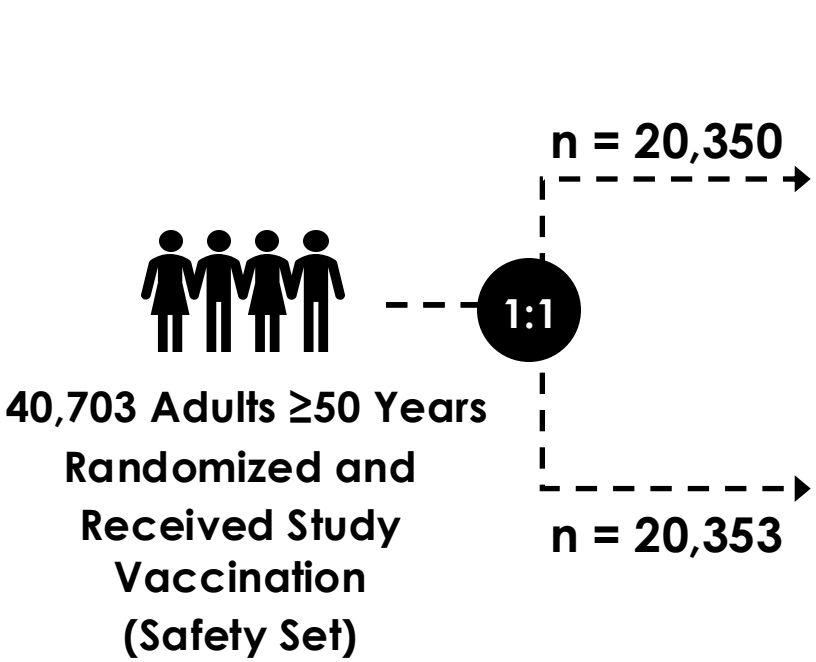
Efficacy and Safety Study Design

Study 304: Randomized, Double-Blind, Active-Controlled Phase 3 Trial (NCT06602024)



mRNA-1010 (37.5 µg TIV)

mRNA Seasonal Influenza Vaccine Candidate

Licensed SD Influenza Vaccine (45 µg TIV or 60 µg QIV)

Licensed Inactivated SD Seasonal Influenza Vaccine

Stratified Randomization:

- Age groups - 50-64 years, ≥65 years[a]
- Influenza vaccine status in previous influenza season (received/not received)

- Follow up through 6 months (Day 181) or end of influenza season, whichever occurred later
- 11 countries and 301 global sites

QIV, quadrivalent; SD, standard dose; TIV, trivalent.
[a]47.8% of participants were ≥65 years; 11.6% of participants were ≥75 years old.
Active comparators include Fluarix (TIV), Fluarix Tetra, Influsplit® Tetra, Alpharix® Tetra.

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Study Objectives

Primary Objectives

- **Noninferiority and superiority of rVE mRNA-1010 vs licensed SD influenza vaccines** against protocol-defined Influenza-Like Illness (ILI) by any influenza A or B strains
- **Safety and reactogenicity** of mRNA-1010

Secondary Objectives

- rVE of mRNA-1010 vs licensed SD influenza vaccine against protocol-defined ILI by **vaccine matched Influenza A and B strains**
- **Immunogenicity in a subset of participants**
- HAI titers as a **surrogate of risk and protection** against RT-PCR-confirmed protocol-defined ILI

Exploratory Objectives

- rVE of mRNA-1010 vs licensed SD influenza vaccine against **medically attended ILI**

CDC, Centers for Disease Control and Prevention; ILI, influenza-like illness; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy
All cases of ILI required RT-PCR confirmation within 7 days of illness onset.

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Influenza-like Illness Case Definitions

Respiratory Illness	• Sneezing, nasal congestion, rhinorrhea, sore throat, cough, sputum production, wheezing, or difficulty breathing
Protocol-Defined ILI	• **≥ 1 systemic symptom:** Oral temperature >37.2°C (>99.0°F), chills, feverish, tiredness, headaches, or myalgia **AND** • **≥ 1 respiratory symptom:** Sore throat, cough, sputum production, wheezing, or difficulty breathing
Modified CDC-Defined ILI	• Oral temperature >37.2°C (>99.0°F), a cough and/or a sore throat

- All cases required **RT-PCR confirmation** within 7 days of illness onset

ILI, influenza-like illness; RT-PCR, reverse transcription polymerase chain reaction.

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Demographics and Baseline Characteristics Were Balanced Between Groups

Safety Set

Characteristic		≥50 Years	
		mRNA-1010 (n = 20,350)	Licensed SD Influenza Vaccines (n = 20,353)
Median age, years		**64**	**64**
Female, n (%)		11,516 (**56.6**)	11,633 (**57.2**)
Age group, n (%)	**50-64 Years**	10,624 (**52.2**)	10,615 (**52.2**)
	≥65 Years	9726 (**47.8**)	9738 (**47.8**)
	≥75 Years	2354 (**11.6**)	2363 (**11.6**)
Vaccinated previous influenza season n (%)		9569 (**47.0**)	9547 (**46.9**)
Race/Ethnicity, n (%)	**White**	16,814 (**82.6**)	16,811 (**82.6**)
	Black or African American	2687 (**13.2**)	2698 (**13.3**)
	Asian	496 (**2.4**)	483 (**2.4**)
	Hispanic/Latino ethnicity	2147 (**10.6**)	2067 (**10.2**)
Frailty in adults aged ≥65 yrs , n (%) (≥4 on Edmonton scale)		2575 (**12.7**)	2583 (**12.7**)
Baseline high-risk conditions, n (%)		11,591 (**57.0**)	11,614 (**57.1**)

- Most common high-risk conditions: diabetes, asthma, obesity (BMI ≥30 kg/m²), chronic obstructive pulmonary disease, atrial fibrillation

BMI, body mass index; SD, standard dose.

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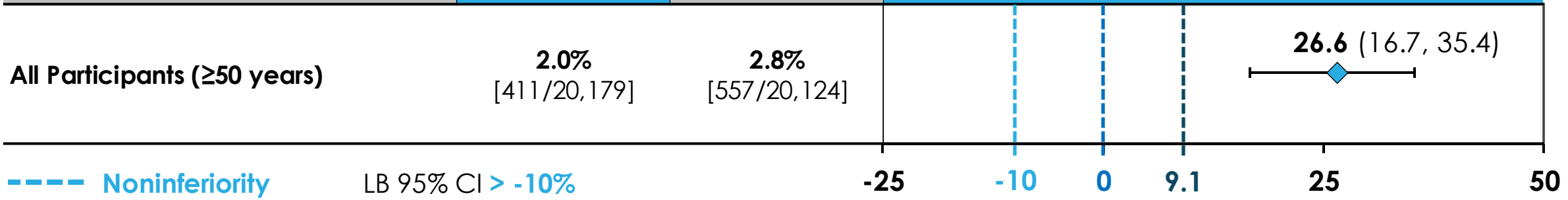
Prespecified Success Criteria Met for rVE of mRNA-1010 vs Licensed SD Influenza Vaccines

Primary Endpoint - Per-Protocol Set (Median 6 months of follow up)

Participants With RT-PCR Confirmed Protocol-Defined ILI Regardless of Influenza Strain, % [n/N]	mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%)[a] (95% CI)
All Participants (≥50 years)	**2.0%** [411/20,179]	**2.8%** [557/20,124]	**26.6** (16.7, 35.4)



- Noninferiority: LB 95% CI **> -10%**
- Superiority: LB 95% CI **> 0**
- Highest Superiority: LB 95% CI **> 9.1%**

Highest Superiority Success Criterion Met

LB of 95% CI >9.1%; 1-sided *P* = 0.0005

CI, confidence interval; ILI, influenza-like illness; LB, lower bound; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy; SD, standard dose.
[a]rVE =100 × (1-hazard ratio [mRNA-1010 vs. active comparator]), hazard ratio estimated using a stratified Cox proportional hazard model (stratified by age group at randomization and previous influenza vaccination status) and with treatment group as a fixed effect.

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Relative Vaccine Efficacy Favorable for mRNA-1010 vs Licensed SD Influenza Vaccines Across Influenza Strains

Per-Protocol Set

Participants With ILI[a] by Influenza Strain,% [n/N]	mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%)[b] (95% CI)
Influenza A H1N1	**1.1%** [223/20,179]	**1.6%** [315/20,124]	**29.6** (16.4, 40.7)
Influenza A H3N2	**0.8%** [158/20,179]	**1.0%** [202/20,124]	**22.2** (4.3, 36.9)
Influenza B Victoria	**0.1%** [25/20,179]	**0.2%** [35/20,124]	**29.1** (-18.5, 57.5)

CI, confidence interval; ILI, influenza-like illness; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy, SD, standard dose

[a]Based on RT-PCR-confirmed protocol-defined ILI

[b]rVE =100 × [1-hazard ratio [mRNA-1010 vs. active comparator]), hazard ratio estimated using a stratified Cox proportional hazard model (stratified by age group at randomization and previous influenza vaccination status) and with treatment group as a fixed effect.

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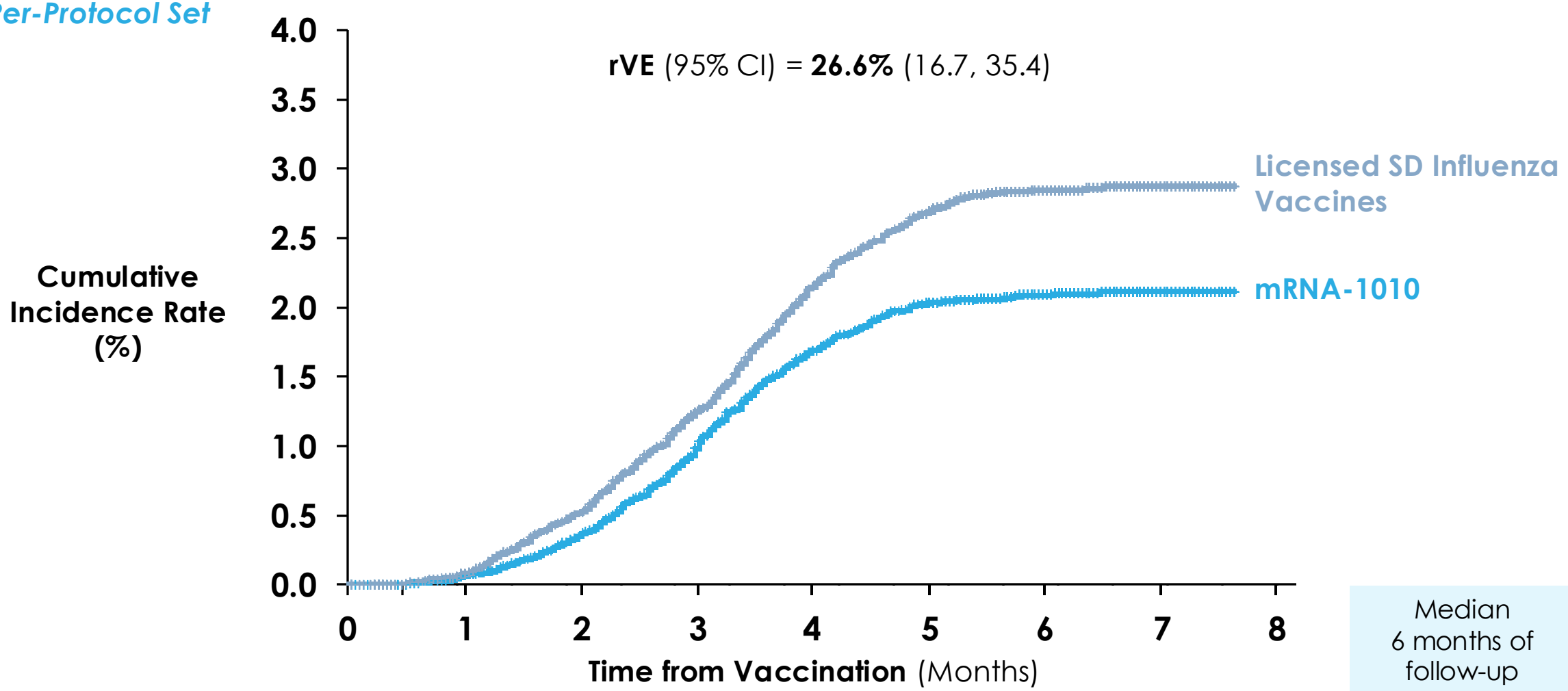
Cumulative Incidence Rates of Influenza-Like Illness Over the 2024-2025 Influenza Season Favored mRNA-1010

Per-Protocol Set



Median 6 months of follow-up

Licensed SD Influenza Vaccines	At Risk	20124	19871	19663	19383	19027	18774	10098	1932	0
	Events	0	16	104	250	428	532	555	557	557
mRNA-1010	At Risk	20179	19930	19765	19506	19151	18925	10180	1962	0
	Events	0	14	74	205	333	400	409	411	411

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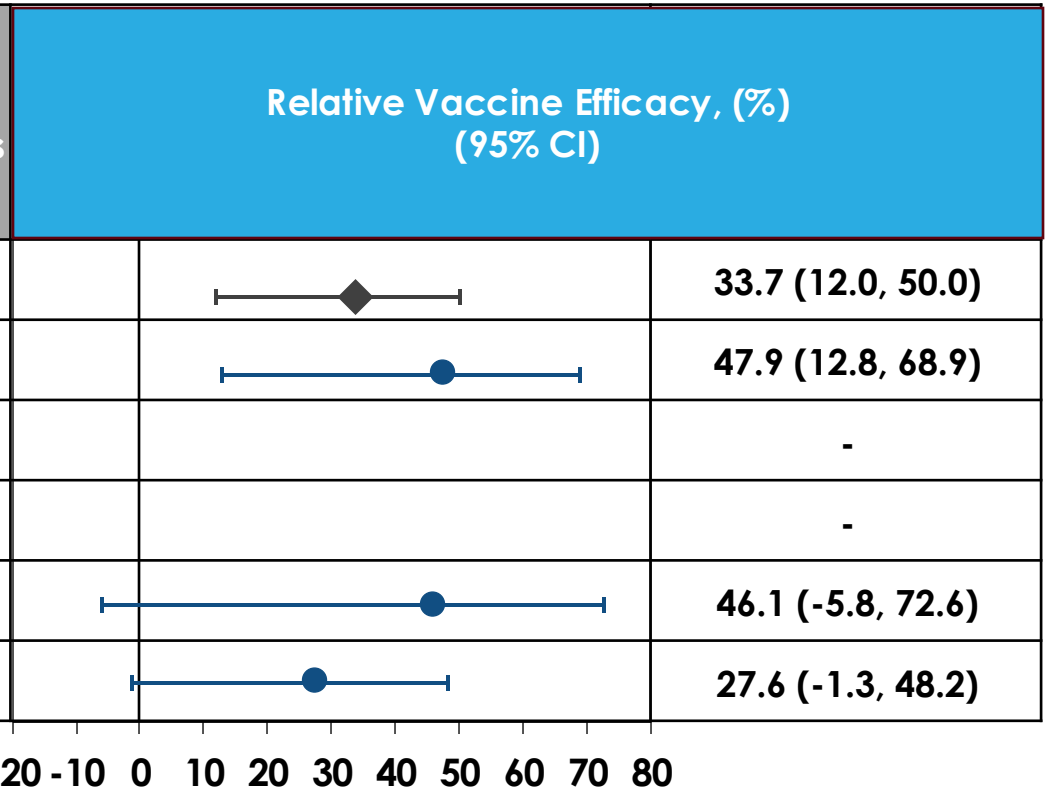
Exploratory Analysis of Medically Attended RT-PCR Confirmed Protocol-Defined ILI in Participants ≥50 Years

Per-Protocol Set

Healthcare Encounters Associated With RT-PCR Confirmed Protocol-Defined ILI, % (n/N)[a]		mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%) (95% CI)
Any healthcare encounter		**0.4%** (80/20,179)	**0.6%** (120/20,214)	**33.7 (12.0, 50.0)**
Seeking a Higher level of Care	**Any**	**0.11%** (22/20,179)	**0.21%**(42/20,214)	**47.9 (12.8, 68.9)**
	Hospitalization	**0.02%** (4/20,179)	**0.04%** (8/20,214)	**-**
	ER visit[b]	**0.03%**(6/20,179)	**0.06%** (12/20,214)	**-**
	Urgent care visit[b]	**0.06%**(13/20,179)	**0.12%** (24/20,214)	**46.1 (-5.8, 72.6)**
Routine clinic	**Outpatient clinic visit**	**0.29%** (59/20,179)	**0.40%** (81/20,214)	**27.6 (-1.3, 48.2)**



CI, confidence interval; ED, emergency department; ILI, influenza-like illness; PP, per-protocol; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy; SD, standard dose.
[a]rVE is calculated based on the healthcare encounters associated with the first RT-PCR-confirmed protocol-defined ILI beginning at least 14 days after study intervention through the end of the influenza season caused by any influenza A or B strains, regardless of vaccine match.
Percentage was based on the total number of participants in the study vaccination PP set. If a case was associated with multiple healthcare encounter types, the participant was counted only once. rVE (95% CI) is not calculated if the total number of cases across both vaccine groups is <20.
[b]ER visits include severe conditions that require immediate medical attention; urgent care visits include less severe conditions that are not an emergency but may require medical attention.[1]
1. Kaiser Permanente. What's the difference between urgent care and emergency care. https://healthy.kaiserpermanente.org/health-wellness/healtharticle.difference-between-urgent-and-emergency-care.

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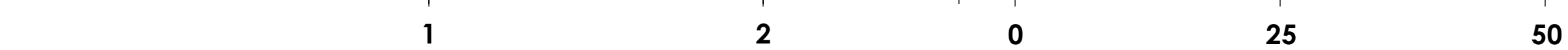
mRNA-1010 Elicited Higher GMR and SCR at Day 29 Compared to Licensed SD Influenza Vaccines (≥50 Years)

Per-Protocol Immunogenicity Subset

Influenza Strains	GMR (95% CI)	SCR Difference (95% CI)
Influenza A H1N1	**1.82** (1.69, 1.97)	**27.9** (24.1, 31.7)
Influenza A H3N2	**1.59** (1.48, 1.71)	**20.0** (16.0, 23.9)
Influenza B Victoria	**1.67** (1.57, 1.78)	**25.3** (21.6, 28.9)



CI, confidence interval; GMR, geometric mean ratio; GMT, geometric mean titer; HA, hemagglutinin; HAI, hemagglutination inhibition; SCR, seroconversion rate; SD, standard dose.
mRNA-1010, n = 1167; licensed SD comparator, n = 1175.
GMR represents mRNA-1010 over SD Influenza comparator; SCR represents mRNA-1010 versus SD Influenza comparator.
HAI assay was identification of influenza virus subtype and detection and quantity of serum HA antibodies to influenza virus.
The log-transformed antibody levels are analyzed using an ANCOVA model, with vaccination group as the fixed variable, log transformed baseline HAI titers as a fixed covariate, adjusting for the randomization stratification factor(s).
The model-based GMT and GMR, and its corresponding 95% CI, are obtained by transforming the least square mean estimate and its CI back to the original scale for presentation.

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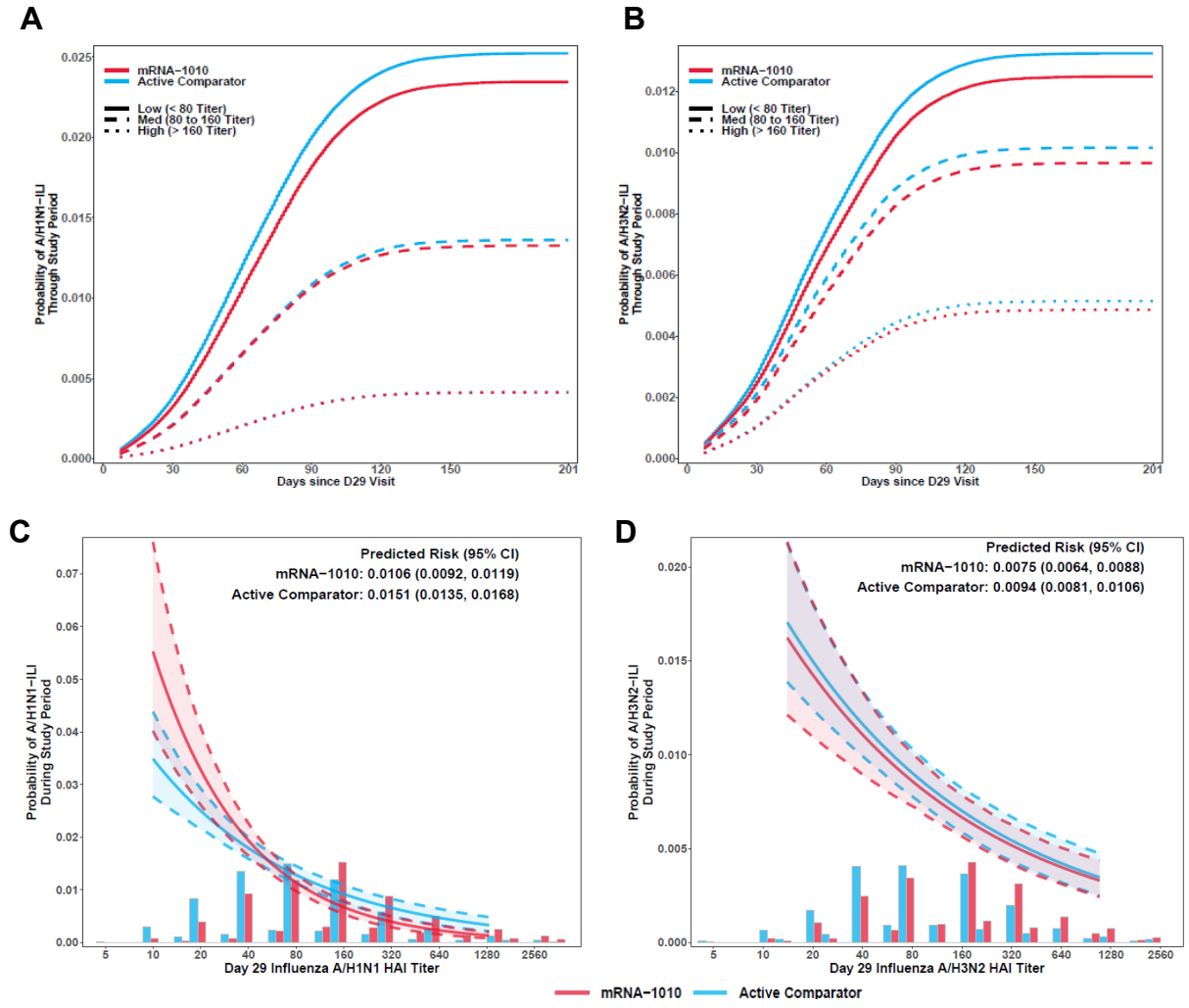
Day 29 HAI Titers Correlate with mRNA-1010 Induced Protection Against ILI

Per-Protocol Correlate Analysis Subset



- Higher Day 29 Strain-Specific HAI Titers (induced by mRNA-1010 or the licensed SD influenza vaccine) correlate with lower ILI risk (Figures A and B)
- Higher Day 29 HAI titers were consistently associated with a reduced risk of ILI in a similar pattern (Figures C and D)

CI, confidence interval; HAI, hemagglutinin inhibition; ILI, influenza-like illness; SD, standard dose.
Figures A and B: Marginalized covariate-adjusted cumulative incidence of A-strain ILI by Day 29 strain-specific HAI titer tertiles by vaccine group was estimated using Cox regression model.
Figures C and D: Solid red (mRNA-1010) and blue (active comparator) curves demonstrate point estimates of the marginalized covariate-adjusted cumulative incidence of A/H1N1 and A/H3N2 ILI endpoints during the study period by mRNA-1010 and the active comparator vaccine across a range of assigned HAI titers (within 2.5th to 97.5th percentilesof observed Day 29 HAI titers in both the mRNA-1010 and the active comparator vaccine groups).

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Safety Data

Safety Set – April 30, 2025 data cutoff

Solicited adverse reaction subset : ~6000 participants

Based on median of 6 months of follow-up

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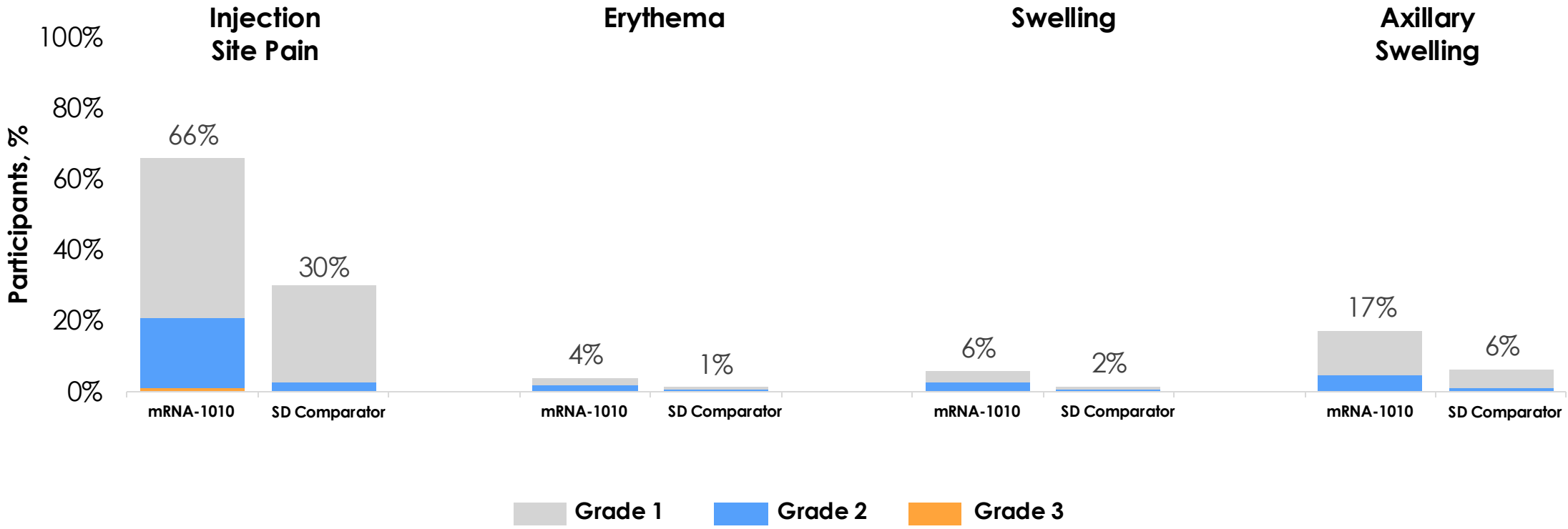
Solicited Local Adverse Reactions for Adults ≥50 Years Within 7 Days of Injection Were Mild to Moderate and of Short Duration

Solicited Safety Set



- Local reactions were higher with mRNA-1010 vs licensed SD comparator
- Low frequency of grade 3 reactions were observed; most reactions grade 1 or 2 and of short duration (median, 2 days)
- Most frequently reported local reaction was injection site pain in both groups
- Fewer, and milder, reactions were reported by participants >75 years in both groups, but the pattern remained similar

SD, standard dose, TIV, trivalent.
mRNA-1010, n = 3015; licensed SD comparator, n = 2997. No grade 4 reactions.
Licensed SD influenza vaccine comapartors included Fluarix (TIV), Fluarix Tetra, Influsplit® Tetra, Alpharix® Tetra

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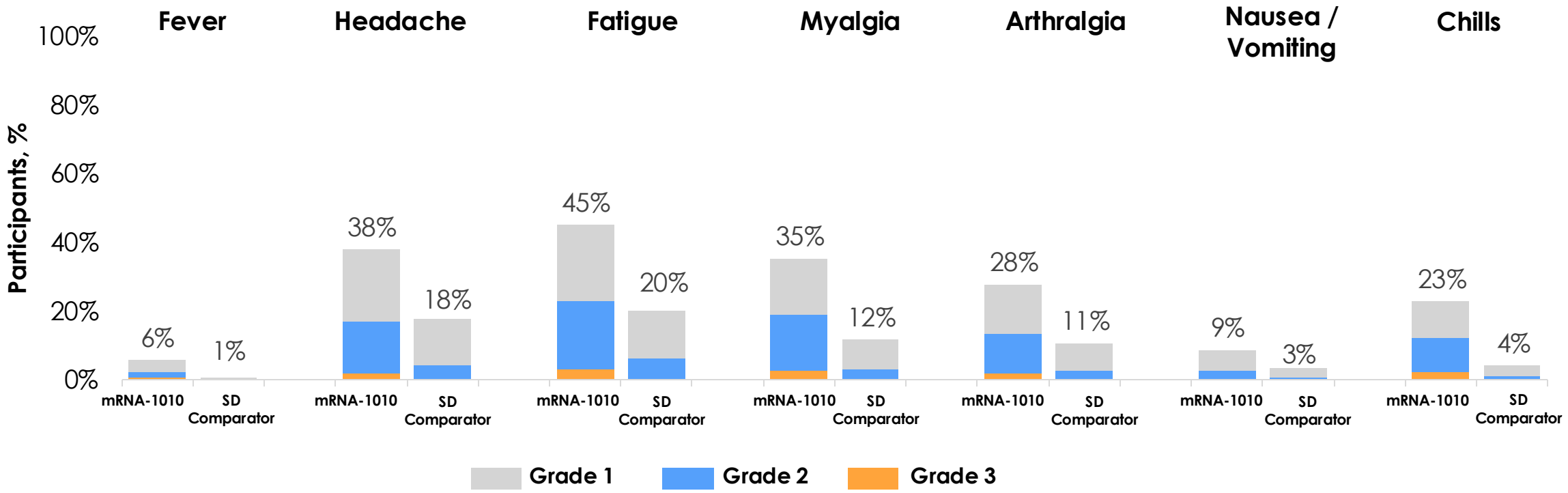
Solicited Systemic Adverse Reactions for Adults ≥50 Years Within 7 Days of Injection Were Mostly Mild to Moderate and of Short Duration

Solicited Safety Set



- Systemic reactions were higher with mRNA-1010 than licensed SD comparator
- Low frequency of grade 3 reactions were observed; most reactions were grade 1 or 2 and of short duration (median, 2 days)
- Most frequently reported systemic reactions were fatigue and headache across both groups
- Fewer, and milder, reactions were reported by participants >75 in both groups, but the pattern remained similar

SD, standard dose; TIV, trivalent.
mRNA-1010, n = 3015; licensed SD comparator, n = 2997. No grade 4 reactions.
Licensed SD influenza vaccine comparators included Fluarix (TIV), Fluarix Tetra, Influsplit® Tetra, Alpharix® Tetra.

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Unsolicited AEs Through 28 Days After Injection Regardless of Relationship Were Similar Between Groups

Safety Set

	≥50 Years	
	mRNA-1010 (n = 20,350)	**Licensed SD Influenza Vaccines** (n = 20,353)
All unsolicited AEs, n (%)	1204 **(5.9%)**	1165 **(5.7%)**
Serious	92 **(0.5%)**	92 **(0.5%)**
Fatal	7 **(<0.1%)**	9 **(<0.1%)**
Medically attended	775 **(3.8%)**	780 **(3.8%)**
Leading to study discontinuation	1 **(<0.1%)**	0
Severe (grade ≥3)	75 **(0.4%)**	77 **(0.4%)**
Severe (grade ≥3), related to study vaccination	1 **(<0.1%)**	1 **(<0.1%)**
Any AE of Special Interest	4 **(<0.1%)**	3 **(<0.1%)**
Myocarditis/Pericarditis/Myopericarditis	0	0

- Frequency of unsolicited AEs was similar between the groups for each category of AEs
- Data from adults aged ≥65 years were comparable

AE, adverse events; SD, standard dose, TIV, trivalent.
Licensed SD influenza vaccine comparators included Fluarix (TIV), Fluarix Tetra, Influsplit® Tetra, Alpharix® Tetra

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Conclusions

Efficacy	• mRNA-1010 showed higher efficacy across age groups, influenza strains, participant subgroups, including participants at high-risk of severe influenza, compared with SD vaccines • Efficacy was maintained over the duration of the influenza season • mRNA-1010 also prevented more severe, medically-attended influenza
Immunogenicity	• Robust immune responses compared to SD influenza vaccines across influenza A and B strains • Similar to other licensed influenza vaccines, Day 29 HAI titers elicited by mRNA-1010 act as surrogate endpoints reasonably likely to predict clinical benefit
Safety	• Reactogenicity was higher with mRNA-1010; however, most solicited adverse reactions were grades 1 or 2 and transient • No safety concerns identified

SD, standard dose.

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