Immunogenicity of an mRNA-Based Seasonal Influenza Vaccine, mRNA-1010, in Adults ≥50 Years

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BACKGROUND

- Globally, seasonal influenza leads to an estimated 3 to 5 million cases of severe illness and 650,000 deaths annually, with the majority of cases occurring in older adults[1]
- Enhanced influenza vaccines, including high-dose (HD), adjuvanted, and recombinant hemagglutinin (HA) formulations, have demonstrated improved immunogenicity and protection in older adults, though protection varies by seasons and circulating strains[2,3]
- Immunogenicity evaluations of influenza vaccines are important, as they can be used as a correlate to vaccine efficacy against circulating influenza strains[4-6]
  - Hemagglutination inhibition (HAI) titers, measured by the HAI assay, are widely recognized as a surrogate marker for protection against influenza infection, with HAI titers of ≥1:40 considered to provide ≥50% reduced risk of influenza illness[4,5]
- mRNA-1010 is an investigational trivalent seasonal influenza vaccine encoding HA antigens from the 3 World Health Organization (WHO)-recommended strains for the 2024-2025 Northern Hemisphere influenza season: A/H1N1, A/H3N2, and B/Victoria[7,8]
- In a phase 3 study (NCT05827978), a single 50-µg dose of mRNA-1010 induced HAI titers against vaccine-matched influenza A and B strains that were statistically superior to those elicited by licensed standard-dose (SD) and HD comparators in adults ≥18 years[7]
- In a pivotal, phase 3, randomized, double-blind, active-controlled, case-driven trial (NCT06602024), mRNA-1010 demonstrated superior relative vaccine efficacy (26.6%; 95% confidence interval [CI], 16.7-35.4) versus a licensed SD influenza vaccine in adults ≥50 years[9]
- Here, we present humoral immunogenicity results from a subset of participants from the pivotal study

OBJECTIVE

- To evaluate the humoral immunogenicity of mRNA-1010 relative to licensed SD active comparators in adults aged ≥50 years from a subset of participants in the pivotal phase 3 efficacy study

METHODS

Study Design

- This phase 3, randomized, observer-blind, active-controlled trial (NCT06602024) evaluated the safety, efficacy, and immunogenicity of mRNA-1010 in adults aged ≥50 years across the Northern Hemisphere
  - Participants were randomly assigned (1:1) to receive a single dose of either mRNA-1010 (37.5 µg total dose; 12.5 µg per influenza strain) or a licensed SD inactivated influenza vaccine comparator (Fluarix, Fluarix Tetra, Influsplit® Tetra, Alpharix® Tetra; GlaxoSmithKline Biologicals, Dresden, Germany)
    - A licensed SD trivalent vaccine (TIV) was the preferred active comparator; however, a licensed quadrivalent vaccine was used in participating countries where a licensed TIV was unavailable
  - The immunogenicity subset included 2394 randomly selected participants who received TIV mRNA-1010 or a licensed TIV comparator, and had baseline and Day 29 HAI data available
    - The subset size was determined based on similarity to powered subsets from previous immunogenicity studies
  - High-risk participants were defined as those with a baseline body mass index ≥30 kg/m² or a medical history of chronic conditions, including autoimmune/immune-mediated, blood, cardiac, pulmonary, renal, hepatic, nervous system, or mental impairment disorders, as well as diabetes mellitus
- This analysis presents the findings on the humoral responses for 3 influenza strains (A/H1N1, A/H3N2, and B/Victoria) based on the WHO recommendations for the 2024-2025 Northern Hemisphere season

HAI Assay

- Humoral responses were evaluated based on a validated HAI assay using guinea pig–derived red blood cells (GP RBCs) and cell-propagated influenza viruses
- The HAI assay was developed based on the WHO method using a standardized input of influenza virus (4 HA units) and a 2-fold serial dilution
- Assay precision, relative accuracy, and dynamic range (lower limit of quantification and upper limit of quantification) were established during validation using a panel of incurred study samples that passed both precision and linearity
- Titer calls were made from GP RBC halos that formed in an event of influenza HA inhibition at a given serum dilution

Study Objectives and Endpoints

- To evaluate the humoral immunogenicity, as measured by the HAI assay, of mRNA-1010 relative to licensed active SD comparators against vaccine-matched influenza A and B strains in a subset of participants. Endpoints included:
  - Geometric mean titer (GMT) at Day 29
  - Geometric mean fold rise (GMFR) comparing Day 29 to Day 1
  - Proportion of participants with an HAI titer ≥1:40 at Day 29
  - Proportion of participants reaching seroconversion at Day 29
  - Seroconversion difference of mRNA-1010 vs TIV comparator at Day 29

RESULTS

Baseline Demographics and Characteristics

- Overall, 2342 participants were included in the per-protocol immunogenicity subset (mRNA-1010, n = 1167; SD comparator, n = 1175; **Table 1**)
- The median age was 64.0 years (range, 50.0-97.0 years); 58.4% of participants were female, 77.9% were White, and 84.2% were non-Hispanic or Latino

Table 1. Participant Demographics and Characteristics in the Per-Protocol Immunogenicity Subset

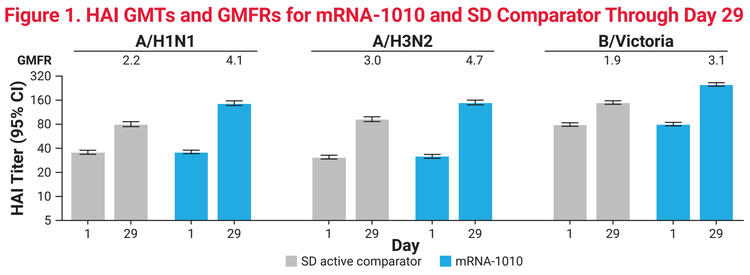
Characteristic	mRNA-1010 (37.5 µg) (n = 1167)	SD Active Comparator (n = 1175)
Median age, years (range)	65.0 (50.0-97.0)	64.0 (50.0-92.0)
Sex, n (%)		
Female	682 (58.4)	685 (58.3)
Age group, n (%)		
50-64 years	581 (49.8)	592 (50.4)
≥65 years	586 (50.2)	583 (49.6)
≥75 years	149 (12.8)	149 (12.7)
Vaccinated previous influenza season, n (%)	594 (50.9)	596 (50.7)
Race/ethnicity, n (%)		
White	914 (78.3)	910 (77.4)
Black or African American	193 (16.5)	200 (17.0)
Asian	27 (2.3)	33 (2.8)
Not Hispanic or Latino	982 (84.1)	991 (84.3)
Frailty ≥65 years, n (%) (≥4 on Edmonton Frail scale)	148 (12.7)	141 (12.0)
≥1 baseline high-risk factor, n (%)	739 (63.3)	752 (64.0)

SD, standard-dose; TIV, trivalent vaccine.
Per-protocol immunogenicity subset included all participants who received the planned dose of TIV study intervention and had no important protocol deviations that impacted the immunogenicity assessment.

Immunogenicity

- At Day 29 post-vaccination, HAI GMTs for mRNA-1010 increased above baseline levels, with GMFRs of 4.07 (95% CI, 3.84-4.31) for A/H1N1, 4.70 (95% CI, 4.44-4.97) for A/H3N2, and 3.14 (95% CI, 2.99-3.31) for B/Victoria (**Figure 1**)
  - While descriptive, Day 29 responses were numerically higher for mRNA-1010 compared with the SD active comparator for all 3 influenza strains

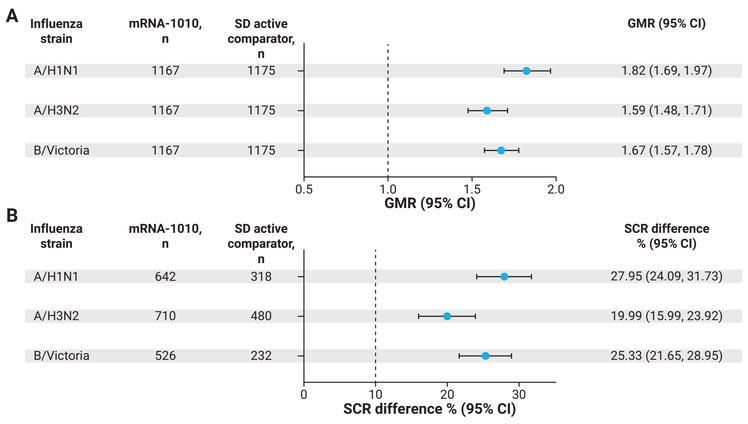
Figure 1. HAI GMTs and GMFRs for mRNA-1010 and SD Comparator Through Day 29



GMFR, geometric mean fold rise; GMT, geometric mean titer; HAI, hemagglutination inhibition; SD, standard-dose; TIV, trivalent vaccine.
Per-protocol immunogenicity subset: mRNA-1010, n = 1167; SD-TIV, n = 1175.
GMFRs at Day 29 from Day 1 (baseline) are shown above each Day 29 bar plot.

- Day 29 GMRs for mRNA-1010 versus SD comparator exceeded 1.4 for all 3 influenza strains (**Figure 2A**); the lower bounds of the 95% CIs for the SCR differences (mRNA-1010 vs SD comparator) all exceeded 15% (**Figure 2B**)

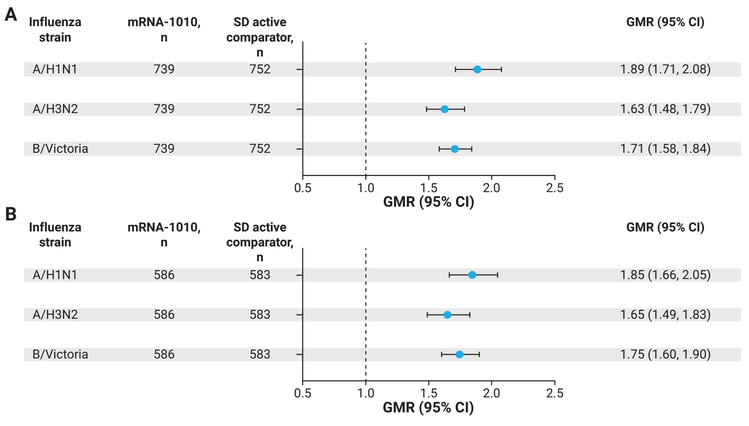
Figure 2. (A) GMR and (B) SCR Difference of Anti-Hemagglutinin Antibodies for mRNA-1010 Versus SD Comparator Through Day 29



CI, confidence interval; GMR, geometric mean titer ratio; HAI, hemagglutination inhibition; LLOQ, lower limit of quantification; SCR, seroconversion rate; SD, standard-dose; ULOQ, upper limit of quantification.
Per-protocol immunogenicity subset.
Antibody values reported as below the LLOQ were replaced by 0.5 ×LLOQ. Values greater than the ULOQ were converted to the ULOQ. Antibody values are shown for A/H1N1 (LLOQ: 10; ULOQ: 3620), A/H3N2 (LLOQ: 10; ULOQ: 2560), and B/Victoria (LLOQ: 10; ULOQ: 1356).
Seroconversion was defined as the proportion of participants having either a post-vaccination titer ≥1:40 if baseline HAI titer was <1:10, or at least a 4-fold rise in post-baseline HAI antibody titer if baseline HAI titer was ≥1:10.
Error bars represent 95% CIs. Dashed lines indicate GMR = 1 (panel A) and SCR difference = 10% (panel B).

- The proportion of participants with a Day 29 HAI titer ≥1:40 was higher in the mRNA-1010 group versus the SD active comparator against all 3 influenza strains (**Table 2**)
- Participants with high-risk factors demonstrated higher antibody responses with mRNA-1010 compared with the SD comparator across all strains, with GMRs of 1.89 (95% CI, 1.71-2.08) for A/H1N1, 1.63 (95% CI, 1.48-1.79) for A/H3N2, and 1.71 (95% CI, 1.58-1.84) for B/Victoria (**Figure 3A**)
- Participants aged ≥65 years also demonstrated higher antibody responses with mRNA-1010 compared with the SD comparator across all strains, with GMRs of 1.85 (95% CI, 1.66-2.05) for A/H1N1, 1.65 (95% CI, 1.49-1.83) for A/H3N2, and 1.75 (95% CI, 1.60-1.90) for B/Victoria (**Figure 3B**)

Figure 3. GMR of Anti-Hemagglutinin Antibodies for mRNA-1010 Versus SD Comparator Through Day 29 in (A) High-Risk Participants and (B) Participants Aged ≥65 Years



CI, confidence interval; GMR, geometric mean titer ratio; LLOQ, lower limit of quantification; SD, standard-dose; ULOQ, upper limit of quantification.
Per-protocol immunogenicity subset.
Antibody values reported as below the LLOQ were replaced by 0.5 ×LLOQ. Values greater than the ULOQ were converted to the ULOQ. Antibody values are shown for A/H1N1 (LLOQ: 10; ULOQ: 3620), A/H3N2 (LLOQ: 10; ULOQ: 2560), and B/Victoria (LLOQ: 10; ULOQ: 1356).
Error bars represent 95% CIs. Dashed lines indicate GMR = 1.

Table 2. Summary of HAI Titers ≥1:40, Seroconversion, and Seroconversion Difference for Vaccine-Matched Seasonal Influenza A and B Strains Measured by HAI Assay by Timepoint (Per-Protocol Immunogenicity Subset)

	A/H1N1	A/H3N2	B/Victoria
HAI titer ≥1:40			
Baseline, n (%)			
mRNA-1010 37.5 µg	651 (55.8)	571 (48.9)	1060 (90.8)
SD active comparator	645 (54.9)	568 (48.3)	1060 (90.2)
Day 29, n (%) [95% CI][a]			
mRNA-1010 37.5 µg	1079 (92.5) [90.79-93.91]	1090 (93.4) [91.82-94.76]	1159 (99.3) [98.65-99.70]
SD active comparator	940 (80.0) [77.6- 82.25]	1008 (85.8) [83.66-87.73]	1151 (98.0) [96.98-98.69]
Day 29 seroconversion, n (%)[b] [95% CI][a]			
mRNA-1010 37.5 µg	642 (55.0) [52.11-57.89]	710 (60.8) [57.97-63.65]	526 (45.1) [42.19-47.98]
SD active comparator	318 (27.1) [24.54-29.70]	480 (40.9) [38.02-43.72]	232 (19.7) [17.50-22.14]
Day 29 SCR difference, % [95% CI][c]			
mRNA-1010 vs SD active comparator	27.95 [24.09-31.73]	19.99 [15.99-23.92]	25.33 [21.65-28.95]

CI, confidence interval; HAI, hemagglutination inhibition; LLOQ, lower limit of quantification; SCR, seroconversion rate; SD, standard-dose; ULOQ, upper limit of quantification.
Per-protocol immunogenicity subset: mRNA-1010, n = 1167; SD active comparator, n = 1175.
Antibody values reported as below the LLOQ were replaced by 0.5 ×LLOQ. Values greater than the ULOQ were converted to the ULOQ. Antibody values are shown for A/H1N1 (LLOQ: 10; ULOQ: 3620), A/H3N2 (LLOQ: 10; ULOQ: 2560), and B/Victoria (LLOQ: 10; ULOQ: 1356).
[a]95% CIs were calculated using the Clopper-Pearson method.
[b]Seroconversion was defined as the proportion of participants having either a post-vaccination titer ≥1:40 if baseline HAI titer was <1:10, or at least a 4-fold rise in post-baseline HAI antibody titer if baseline HAI titer ≥1:10.
[c]95% CIs were calculated using the Miettinen-Nurminen (score) method.

CONCLUSIONS

- A single dose of mRNA-1010 elicited a robust antibody response against all vaccine-matched strains in adults aged ≥50 years
- Immune responses were higher for mRNA-1010 than the SD comparator, consistent with prior findings in adults ≥65 years where mRNA-1010 was demonstrated superior to HD influenza vaccination[5]
- Robust immune responses were also observed in participants with high-risk factors and aged ≥65 years across all strains
- Taken together with efficacy and safety results, these data support mRNA-1010 as a potential enhanced influenza vaccine candidate in adults ≥50 years

References

1. WHO. Influenza (Seasonal). Accessed September 17, 2025. https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)
2. Chaves SS, et al. *Clin Infect Dis*. 2023;77(7):1032-1042. doi:10.1093/cid/ciad322
3. Youhanna J, et al. *Influenza Other Respir Viruses*. 2024;18(4):e13286. doi:10.1111/irv.13286
4. Yamayoshi S, Kawaoka Y. *Nat Med*. 2019;25(2):212-220. doi:10.1038/s41591-018-0340-z
5. Reber A, Katz J. *Expert Rev Vaccines*. 2013;12(5):519-536. doi:10.1586/erv.13.35
6. Kandinov B, et al. *Hum Vaccin Immunother*. 2025;21(1):2484088. doi:10.1080/21645515.2025.2484088
7. Soens M, et al. *Vaccine*. 2025;50:126847. doi:10.1016/j.vaccine.2025.126847
8. WHO. Recommended Composition of Influenza Virus Vaccines for Use in the 2024-2025 Northern Hemisphere Influenza Season. Accessed September 17, 2025. https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2024-2025-northern-hemisphere-influenza-season
9. Moderna Announces Positive Phase 3 Results for Seasonal Influenza Vaccine. June 30, 2025. https://www.accessnewswire.com/newsroom/en/healthcare-and-pharmaceutical/moderna-announces-positive-phase-3-results-for-seasonal-influenza-vac-1044119

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Disclosures

EW, BF, H-LC, RC, AA, and RD are employees of Moderna, Inc., and may hold stock/stock options in the company.

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