P0096

Six-month persistence and safety of mRNA-based influenza or multicomponent influenza/COVID-19 vaccines versus licensed comparators in adults aged ≥18 years

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BACKGROUND

- Seasonal influenza and SARS-CoV-2 viruses are global health concerns responsible for substantial disease burden[1,2]
- mRNA vaccine technology allows for quick updates in vaccine composition to match circulating strains due to the rapid manufacturing timeline[3]
- The investigational mRNA-1010 influenza vaccine contains mRNAs encoding haemagglutinin surface glycoproteins of seasonal influenza strains recommended by the World Health Organization[4]
  - In a phase 3 study among adults aged ≥18 years (P303; NCT05827978), a single dose of mRNA-1010 induced strong immune responses at Day 29 against seasonal influenza A and B strains that were superior to licensed standard-dose and high-dose influenza vaccines, with an acceptable safety profile[4]
- The investigational multicomponent vaccine mRNA-1083 combines the components of mRNA-1010 with a second-generation COVID-19 vaccine, mRNA-1283, which demonstrated noninferior efficacy than the first-generation COVID-19 vaccine (mRNA-1273) in adults aged ≥18 years in a phase 3 trial[5]
  - In a phase 3 study among adults aged ≥50 years (P301; NCT06097273), a single dose of mRNA-1083 induced strong immune responses at Day 29 against seasonal influenza A and B and SARS-CoV-2 strains, which were superior to licensed standard-dose influenza and COVID-19 vaccines in adults aged 50-64 years, and noninferior to licensed high-dose influenza and COVID-19 vaccines in adults aged ≥65 years, with an acceptable safety profile[6]

OBJECTIVE

- To evaluate the 6-month immunogenicity and safety from two phase 3 studies of mRNA-based standalone vaccine against seasonal influenza (mRNA-1010) or multicomponent vaccine against seasonal influenza + COVID-19 (mRNA-1083)

METHODS

Study Design and Population

mRNA-1010 P303 Study (NCT05827978)

- The P303 trial was a 3-part, phase 3, randomised, observer-blind, active-controlled study conducted across 103 US sites
  - Part A: Participants aged ≥18 years were randomly assigned to receive either a single dose of mRNA-1010 or licensed standard-dose inactivated influenza vaccine, quadrivalent (SD-IIV4)
  - Part B: Participants aged 18-64 years were randomly assigned to receive either a single dose of mRNA-1010 or licensed SD-IIV4
  - Part C: Participants aged ≥65 years were randomly assigned to receive either a single dose of mRNA-1010 or licensed high-dose inactivated influenza vaccine, quadrivalent (HD-IIV4)

mRNA-1083 P301 Study (NCT06097273)

- The P301 trial was a phase 3, randomised, observer-blind, active-controlled study, including 2 age-cohort substudies, conducted across 146 US sites
  - Cohort A: Participants aged ≥65 years were randomly assigned to receive mRNA-1083 + placebo or licensed HD-IIV4 + COVID-19 vaccine
  - Cohort B: Participants aged 50-64 years were randomly assigned to receive mRNA-1083 + placebo or licensed SD-IIV4 + COVID-19 vaccine

Immunogenicity Assessments

- Blood samples for immunogenicity assessments were collected from all participants at baseline (Day 1) and Day 29, and from a participant subset at Day 181
- Haemagglutination inhibition assay (HAI) assessed immune responses to vaccine-matched strains of influenza A/H1N1, A/H3N2, B/Victoria, and B/Yamagata, utilising cell-grown live viruses
- Pseudovirus neutralisation assay (PsVNA) assessed immune responses to a vaccine-matched strain of SARS-CoV-2 (XBB.1.5)

Safety Assessments

- Solicited local or systemic adverse reactions (ARs) were recorded for 7 days after vaccination
- Unsolicited adverse events (AEs) were collected for 28 days after vaccination
- Serious AEs, AEs of special interest (AESIs), medically attended AEs, and AEs leading to study discontinuation were collected throughout study duration (to Day 181)

RESULTS

Study Populations

- Participant demographics in the mRNA-1010 and mRNA-1083 phase 3 studies were generally reflective of the US population and were well balanced across vaccine groups within each study part/cohort (**Table 1**)

Table 1. Participant Demographics

	mRNA-1010 study[a,b]					
	Part A: ≥18 years		Part B: 18-64 years		Part C: ≥65 years	
	mRNA-1010 N = 1220	SD-IIV4 N = 1180	mRNA-1010 N = 1492	SD-IIV4 N = 1488	mRNA-1010 N = 1502	HD-IIV4 N = 1490
Median age (min, max), years	50 (18, 86)	50 (18, 91)	49 (18, 64)	50 (18, 64)	70 (65, 93)	70 (64, 93)
Female	660 (54.1)	623 (52.8)	877 (58.8)	904 (60.8)	878 (58.5)	852 (57.2)
White	919 (75.3)	851 (72.1)	1012 (67.8)	966 (64.9)	1255 (83.6)	1220 (81.9)
Black/African American	248 (20.3)	270 (22.9)	420 (28.2)	444 (29.8)	224 (14.9)	235 (15.8)
Not Hispanic/ Latino ethnicity	937 (76.8)	940 (79.7)	1073 (71.9)	1079 (72.5)	1037 (69.0)	1021 (68.5)
Received influenza vaccine in prior season	484 (39.7)	457 (38.7)	512 (34.3)	496 (33.3)	488 (32.5)	496 (33.3)

	mRNA-1083 study[a,c]			
	Cohort A: ≥65 years		Cohort B: 50-64 years	
	mRNA-1083 N = 2011	HD-IIV4 + mRNA-1273 N = 2006	mRNA-1083 N = 1993	SD-IIV4 + mRNA-1273 N = 2005
Median age (min, max), years	70 (67, 74)	70 (67, 74)	58 (54, 61)	58 (54, 61)
Female	1078 (53.6)	1098 (54.7)	1156 (58.0)	1194 (59.6)
White	1577 (78.4)	1565 (78.0)	1374 (68.9)	1344 (67.0)
Black/African American	370 (18.4)	370 (18.4)	516 (25.9)	551 (27.5)
Not Hispanic/ Latino ethnicity	1688 (83.9)	1689 (84.2)	1576 (79.1)	1603 (80.0)
Received influenza vaccine in prior season	1019 (50.7)	1016 (50.6)	784 (39.3)	784 (39.1)
Received COVID-19 vaccine in prior season	854 (42.5)	853 (42.5)	631 (31.7)	611 (30.5)

HD, high dose; IIV4, inactivated influenza vaccine, quadrivalent; max, maximum; min, minimum; SD, standard dose.

Data are presented as n (%) unless otherwise specified.

[a]The safety population consisted of all participants who were randomly assigned and received any study vaccine.

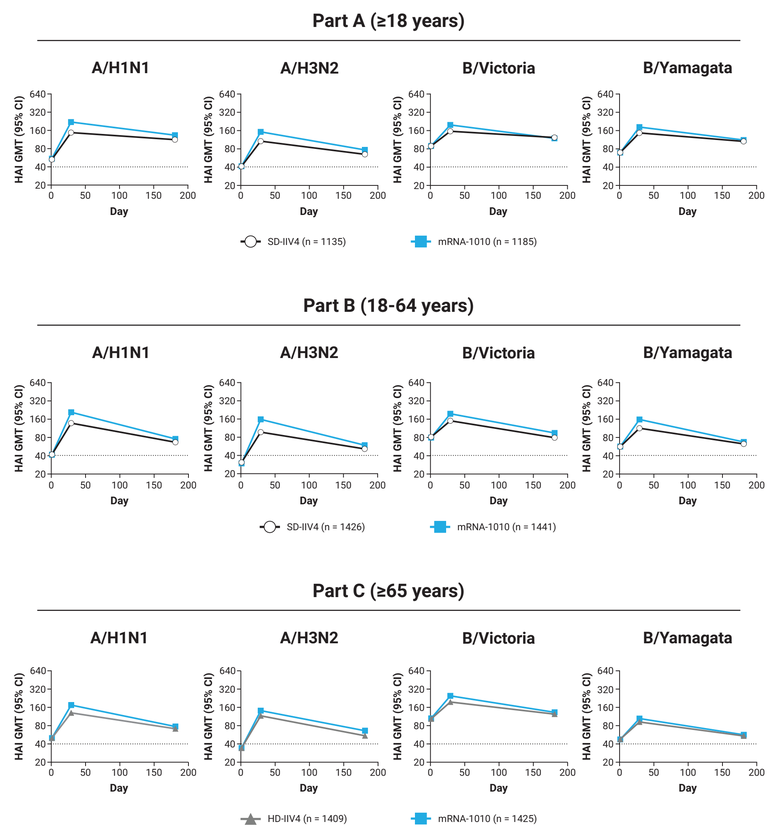
[b]Random assignment to vaccine groups in Part A was stratified by age group (18-49 years, 50-64 years, or ≥65 years) and by receipt of influenza vaccine in the prior 12 months (received or not received). Random assignment in Parts B and C was stratified by receipt of influenza vaccine since September 2022 (received or not received and, if received, whether or not it was from participation in the mRNA-1010-P302 study [NCT05566639]).

[c]In both age cohort substudies of the mRNA-1083 P301 study, random assignment to vaccine groups was stratified by receipt of influenza vaccine since September 2022 (received or not received). Additionally, random assignment in the ≥65 years substudy was stratified into 65-74 or ≥75 years age groups.

mRNA-1010 Immunogenicity

- In Parts A-C of the mRNA-1010 study, HAI titres to all 4 vaccine-matched influenza strains remained above baseline through 6 months (Day 181) post-vaccination with mRNA-1010 or licensed standard-dose or high-dose influenza vaccines **(Figure 1)**
  - mRNA-1010 elicited HAI titres at Day 29 that were higher than those elicited by licensed SD-IIV4 or HD-IIV4 comparators for all vaccine-matched influenza strains; titres were numerically similar to or higher than comparators for all age groups at 6 months post-vaccination

Figure 1. Influenza HAI GMTs Through 6 Months in the mRNA-1010 Study



GMT, geometric mean titre; HAI, haemagglutination inhibition assay; HD, high dose; IIV4, inactivated influenza vaccine, quadrivalent; SD, standard dose.

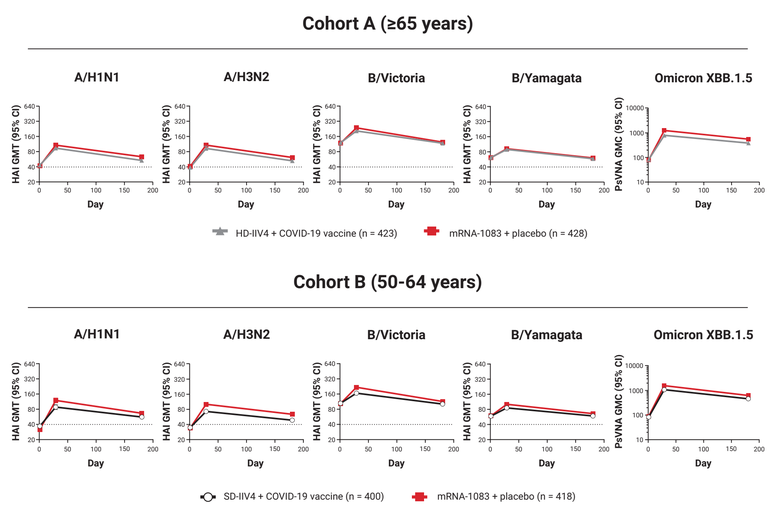
Per-protocol immunogenicity population.

Horizontal dotted line indicates the HAI GMT associated with a 50% reduction in risk of influenza infection in healthy adults.

mRNA-1083 Immunogenicity

- In Cohorts A and B of the mRNA-1083 study, HAI titres to all 4 vaccine-matched influenza strains remained above or similar to comparator through 6 months (Day 181) post-vaccination with mRNA-1083 **(Figure 2)**
- PsVNA concentrations to the vaccine-matched SARS-CoV-2 strain (XBB.1.5) remained higher than comparator through 6 months (Day 181) post-vaccination with mRNA-1083 in both cohorts

Figure 2. Influenza HAI GMTs and SARS-CoV-2 Omicron XBB.1.5 PsVNA GMCs Through 6 Months in the mRNA-1083 Study



GMC, geometric mean concentration; GMT, geometric mean titre; HAI, haemagglutination inhibition assay; HD, high dose; IIV4, inactivated influenza vaccine, quadrivalent; PsVNA, pseudovirus neutralisation assay; SD, standard dose.

Per-protocol immunogenicity population subset who provided immunogenicity blood sampling at Day 181.

Horizontal dotted line indicates the HAI GMT associated with a 50% reduction in risk of influenza infection in healthy adults.

Safety

- Most solicited local or systemic ARs within 7 days after mRNA-1010 or mRNA-1083 vaccination were grade 1 or 2 in severity
  - Median duration of local or systemic ARs was 2-3 days across mRNA vaccine and active comparator groups
  - Injection site pain was the most commonly reported local AR; headache, fatigue, and myalgia were the most commonly reported systemic ARs
- In the mRNA-1010 study, the proportion of participants with any unsolicited AE of any cause occurring within 6 months post-vaccination was 23.0% (A), 18.5% (B), and 20.6% (C) for mRNA-1010, and 21.5% (A), 18.7% (B), and 19.5% (C) for active comparator
  - Few participants had serious AEs (2.2% [A], 1.7% [B], and 2.7% [C] for mRNA-1010; 1.8% [A], 1.5% [B], and 2.6% [C] for comparator)
  - AESIs classified by the investigator as having a relationship to the study vaccination were Bell's palsy in 1 (<0.1%) mRNA-1010 recipient (B) and face swelling in 1 (<0.1%) mRNA-1010 recipient (C); there were no related AESIs of myocarditis or pericarditis
- In the mRNA-1083 study, the proportion of participants with any unsolicited AE of any cause occurring within 6 months post-vaccination was 25.0% (A) and 18.9% (B) for mRNA-1083, and 24.9% (A) and 18.8% (B) for active comparator
  - Few participants had serious AEs (3.5% [A] and 1.5% [B] for mRNA-1083; 2.6% [A] and 1.3% [B] for comparator)
  - An AESI of confusional state in 1 (<0.1%) mRNA-1083 recipient (A) was classified by the investigator as having a relationship to the study vaccination; however, this was not a protocol-defined AESI and there were several confounders (ie, advanced age, history of post-traumatic stress disorder and hypertension, and concurrent SARS-CoV-2 infection)
  - There were no related AESIs of myocarditis or pericarditis

CONCLUSIONS

- In these two phase 3 studies, mRNA-1010 (seasonal influenza) and mRNA-1083 (seasonal influenza + COVID-19) elicited robust humoral immune responses against vaccine-matched strains that persisted through 6 months post-vaccination, remaining comparable to or higher than licensed vaccine comparators
- For both mRNA-1010 and mRNA-1083 vaccines (N = 4214 and N = 4004, respectively), acceptable tolerability and safety profiles were observed over the 6-month period of follow-up
- These findings support the potential of mRNA-based standalone vaccination against seasonal influenza or multicomponent vaccination against seasonal influenza + COVID-19 and could represent a meaningful benefit for global public health

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Disclosures

MS, DH, AKRS, AF, SO, AB, RC, WD, IW, ED, BG, AA, BC, RN, HZ, RD, EW, and LK are employees of Moderna, Inc., and may hold stock or stock options in the company.

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