Safety and Immunogenicity of mRNA-1018, a Candidate Vaccine for the Prevention of H5N1 Pandemic Influenza, in Healthy Adults ≥18 Years of Age in a Dose Ranging Phase 1/2 Clinical Study

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Background

- Influenza A viruses remain a persistent pandemic threat due to their zoonotic potential and capability of antigenic shift, enabling the emergence of novel strains with pandemic potential[1,2]
- H5N1, an influenza A subtype, causes infections in birds and mammals; however, rare but severe infections in humans have been documented[3]
  - Since 2024, 70 A(H5N1) human infections have been reported in the US[4]
  - Mutational events and genomic reassortment increase the risk of human adaptation and pandemic potential[5,6]
- Vaccination may be the most effective method to mitigate disease severity and reduce the risk of a future pandemic[3,7]
- mRNA technology offers advantages over traditional platforms, allowing rapid development of vaccines to address emerging health threats[8,9]
- Decades of research culminated in the clinical implementation of mRNA vaccines during the COVID-19 pandemic, where mRNA vaccines demonstrated safety and efficacy in large phase 3 clinical trials[10]
- In a phase 3 study in adults aged ≥50 years, mRNA-1010, an investigational seasonal influenza vaccine, demonstrated superior relative vaccine efficacy compared to a licensed standard-dose seasonal influenza vaccine[11]
  - These results will be presented in an oral presentation 229 titled "mRNA-1010, an mRNA-Based Influenza Vaccine, is Safe and Efficacious in Adults Aged ≥50 Years" on October 20, 2025 at IDWeek
- A vaccine candidate, mRNA-1018, encoding H5 hemagglutinin (HA) of A/chicken/Ghana/2021, a World Health Organization candidate vaccine virus[12], is currently under clinical investigation for H5N1 pandemic influenza prevention

We present findings from a phase 1/2 trial that assessed the reactogenicity, safety and immunogenicity of mRNA-1018 among healthy adults aged ≥18 years

1. Centers for Disease Control and Prevention. Types of Influenza Viruses. https://www.cdc.gov/flu/about/viruses-types.html. 2. Mostafa A, et al. *Viruses*. 2018;10(9):497. 3. World Health Organization. Influenza: A(H5N1). https://www.who.int/news-room/questions-and-answers/item/influenza-h5n1#:~:text=H5N1%20influenza%20virus%20infection%20can%20cause%20a%20range,and%20other%20non-respiratory%20symptoms%20have%20also%20been%20reported. 4. Centers for Disease Control and Prevention. H5 Bird Flu: Current Situation. https://www.cdc.gov/bird-flu/situation-summary/index.html. 5. Centers for Disease Control and Prevention. Global Summary of Recent Human Cases of H5N1 Bird Flu. https://www.cdc.gov/bird-flu/spotlights/h5n1-summary-08042025.html. 6. The Lancet Regional Health –Americas. 2025;46:101150. 7. Chiba S, et al. *NPJ Vaccines*. 2024;9(1):189. 8. Leong KY, et al. *Virology J*. 2025;22(1):71. 9. Dolgin E. *Nat Rev Drug Discov*. 2021;20(11):801-803. 10. Iqbal SM, et al. *Front Public Health*. 2024;12:1429265. 11. Moderna Press Release. Moderna Announces Positive Phase 3 Results for Seasonal Influenza Vaccine. https://feeds.issuerdirect.com/news-release.html?newsid=489932652116426 6&symbol=MRNA. 12. World Health Organization. Summary of Status of Development and Availability of A(H5N1) Candidate Vaccine Viruses and Potency Testing Reagents. https://cdn.who.int/media/docs/default-source/cvv-southern-hemisphere-2025/h5n1_summary_a_h5n1_cvv_20240927.pdf?sfvrsn=f7f9ff20_1.

Phase 1/2 Study of mRNA-1018 in Adults (NCT05972174)

A Randomized, Dose-ranging, Observer-Blind, Parallel, Multicenter Study Evaluating Safety, Reactogenicity and Immunogenicity of mRNA-1018 in Adults: Results for Part B of the study

Participants
1500 adults aged ≥18 years were randomized to receive 2 doses of mRNA-1018 containing either H5N8, H5 only, H7N9, or H7 only (Part A) or **mRNA-1018 containing H5 only-CG (Part B), administered 21 days apart**

Objectives
Primary objective: To evaluate the safety and tolerability of group 1 and 2 HA and HA+NA mRNA-1018 vaccine at various dose levels in healthy adults ≥18 years

Secondary objectives: To evaluate humoral immune response by hemagglutination inhibition (HAI), microneutralization (MN), NA inhibition (NAI), and cellular immunogenicity (CMI)

Duration
Participants followed up for 6 months after last dose (study initiated in July 2023)

Site Locations
United States and United Kingdom

	Influenza A Group 1 vaccine	*Influenza A Group 2 vaccine*
Part A	**Arm 1: H5N8 / HA+NA** (25 µg) N = 100	**Arm 7: H7N9 / HA+NA** (25 µg) N = 100
	Arm 2: H5N8 / HA+NA (50 µg) N = 100	**Arm 8: H7N9 / HA+NA** (50 µg) N = 100
	Arm 3: H5N8 / HA+NA (100 µg) N = 100	**Arm 9: H7N9 / HA+NA** (100 µg) N = 100
	Arm 4: H5 only / HA only (12.5 µg) N = 100	**Arm 10: H7 only / HA only** (12.5 µg) N = 100
	Arm 5: H5 only / HA only (25 µg) N = 100	**Arm 11: H7 only / HA only** (25 µg) N = 100
	Arm 6: H5 only / HA only (50 µg) N = 100	**Arm 12: H7 only / HA only** (50 µg) N = 100

	Influenza A Group 1 vaccine
Part B	**Arm 13: H5 only-CG / HA only** (12.5 µg) N = 100
	Arm 14: H5 only-CG / HA only (25 µg) N = 100
	Arm 15: H5 only-CG / HA only (50 µg) N = 100

- Sequence(s) for Part A arms (HA and NA) are based on **A/Astrakhan/3212/2020 (H5N8)** and **A/Anhui/1/2013 (H7N9)**
- Sequence for Part B arms (HA only) is based on **A/chicken/Ghana/AVL-763_21VIR7050-39/2021 (H5)**
  - **H5 strains in the study are part of the same clade and antigenically similar to the viruses currently circulating in the US**

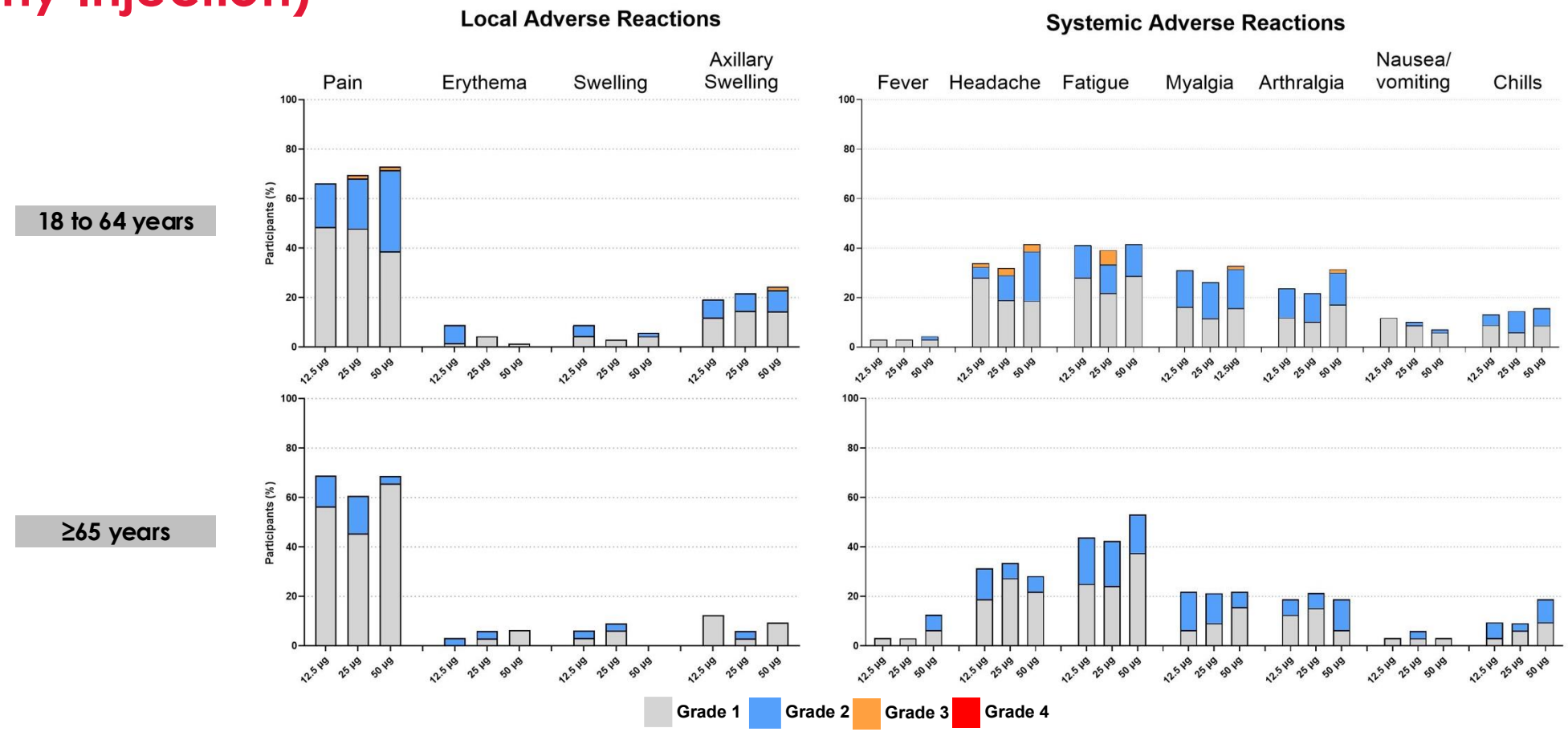
CG, chicken Ghana; HA, hemagglutinin; NA, neuraminidase.

Disposition and Demographics of Participants Who Received mRNA-1083 (H5-CG)

- **A total of 304 participants were included in the randomization set**
  - Randomization was stratified by age (18 – 64 years [n = 207] and ≥65 years [n = 97])
  - All participants (n = 304 [100%]) received **injection 1** (mRNA-1018 12.5 µg, n = 100; mRNA-1018 25 µg, n = 102; mRNA-1018 50 µg, n = 102)
  - 292 (96.1%) participants received **injection 2** (mRNA-1018 12.5 µg, n = 97; mRNA-1018 25 µg, n = 99; mRNA-1018 50 µg, n = 96)
- **Overall, 274 participants completed Part B of the study**
  - Reasons for discontinuation included lost to follow-up (n = 18) and withdrawal of consent (n = 12)
- **The median (min, max) age of participants was 54.5 (18, 82) years; most participants were female (n = 178 [58.6%]), White (n = 233 [76.6%]), and non-Hispanic or Latino (n = 214 [70.4%])**

Max, maximum; min, minimum.

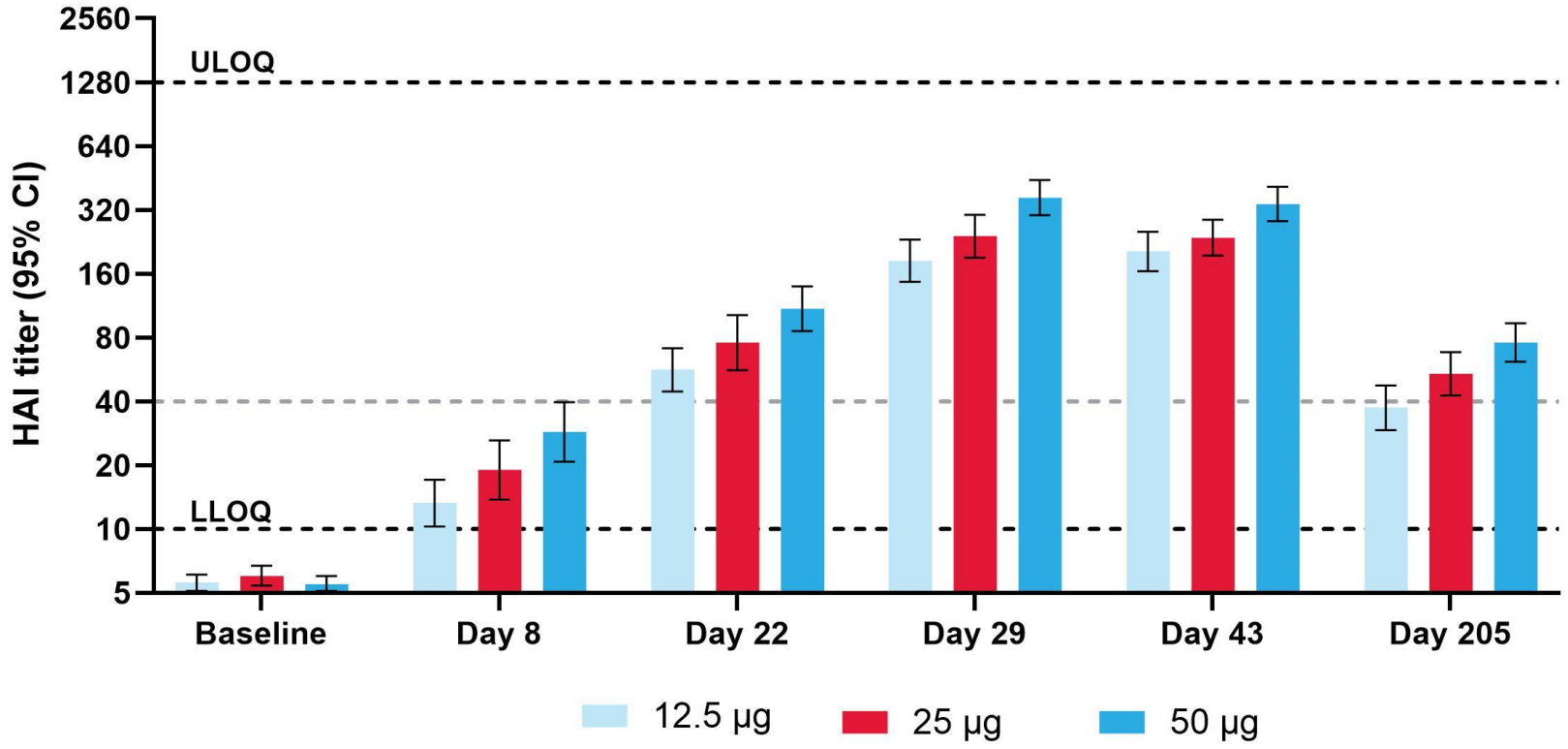
Reactogenicity and Safety of mRNA-1018 (H5-CG) by Age Group (Any Injection)



- Most solicited local and systemic ARs were grade 1 or 2 in severity; no grade 4 events were reported
- Pain at the injection site was the most commonly reported local AR; fatigue and headache were the most commonly reported systemic ARs
- Most unsolicited AEs were not considered vaccine-related up to 21 days after vaccination; on Day 23, 1 related SAE (syncope) was reported. The event was recovered/resolved on Day 25, and was assessed as not related to study treatment by the Sponsor

AE, adverse event; AR, adverse reaction; CG, chicken Ghana; eDiary, electronic diary; SAE, serious adverse event.
Figure presents local and systemic ARs within 7 days after either injection by grade.
Solicited safety set consisted of participants in the safety set who contributed any solicited AR data (had at least 1 post-baseline eDiary assessment). Aged 18 to 64 years: mRNA-1018 (12.5 µg), n = 68; mRNA-1018 (25 µg), n = 69; mRNA-1018 (50 µg), n = 70. Aged ≥65 years: mRNA-1018 (12.5 µg), n = 32; mRNA-1018 (25 µg), n = 33; mRNA-1018 (50 µg), n = 32.

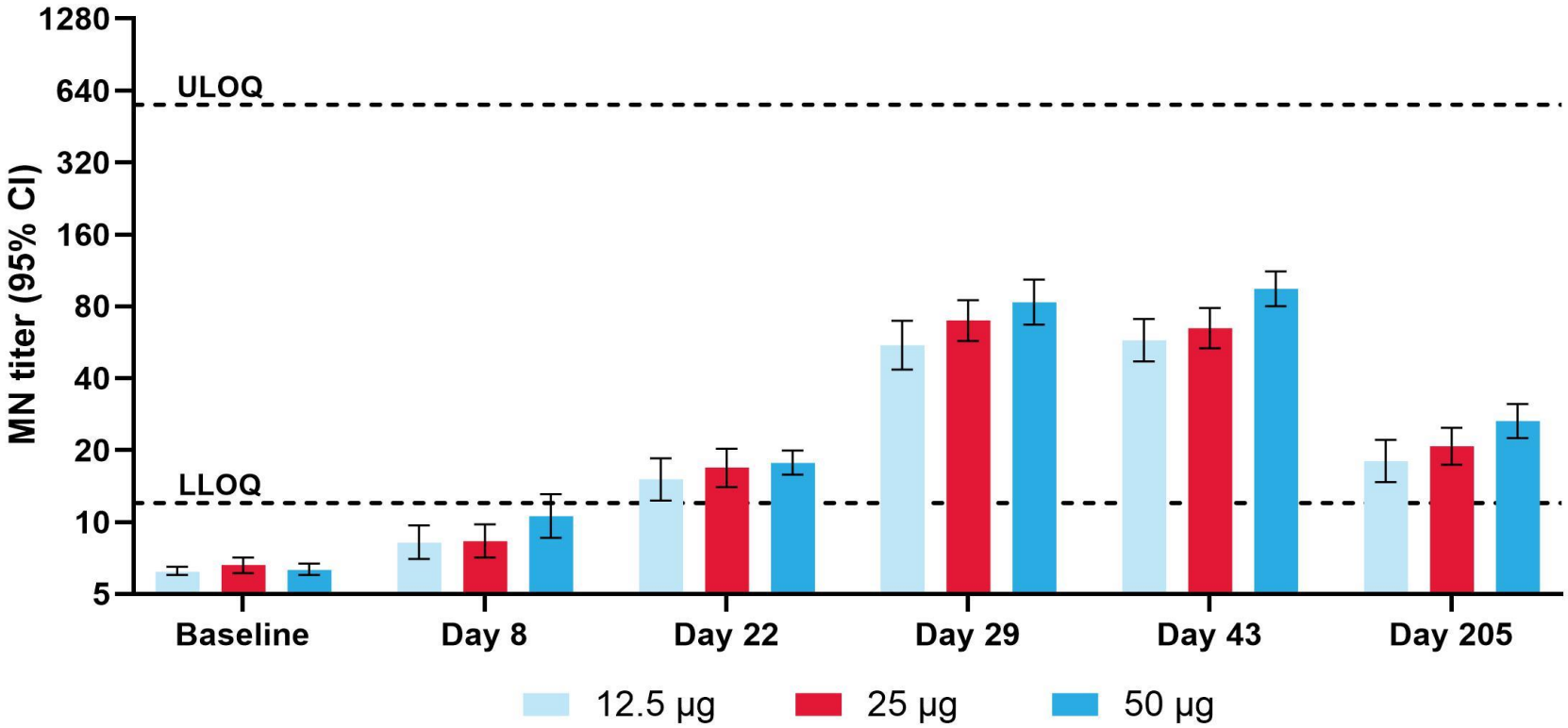
HAI Titers in the Overall Population After Vaccination with mRNA-1018 (H5-CG)



- In the overall population, GMTs were detected at Day 8, peaked at Days 29 or 43, and remained detectable through Day 205
- Higher GMTs were induced with increasing mRNA-1018 dose
- Three weeks after the second dose, the percentage of participants in all dose groups with HAI titers ≥1:40 (defined as seroprotection) were 97.8% (95% CI; 95.4, 99.2)

CI, confidence interval; CG, chicken Ghana; GMT, geometric mean titer; HAI, hemagglutination inhibition; LLOQ, lower limit of quantification; ULOQ, upper limit of quantification.
Per-protocol immunogenicity set. Overall: Baseline, n = 283; Day 8, n = 282; Day 22, n = 283; Day 29, n = 273; Day 43, n = 278; Day 205, n = 269.
Antibody values reported as below the LLOQ were replaced with 0.5 × LLOQ; values greater than the ULOQ were converted to the ULOQ. LLOQ = 10; ULOQ = 1280. Bars indicate GMT with 95% CI. Gray dashed line indicates 1:40 titer associated with seroprotection.

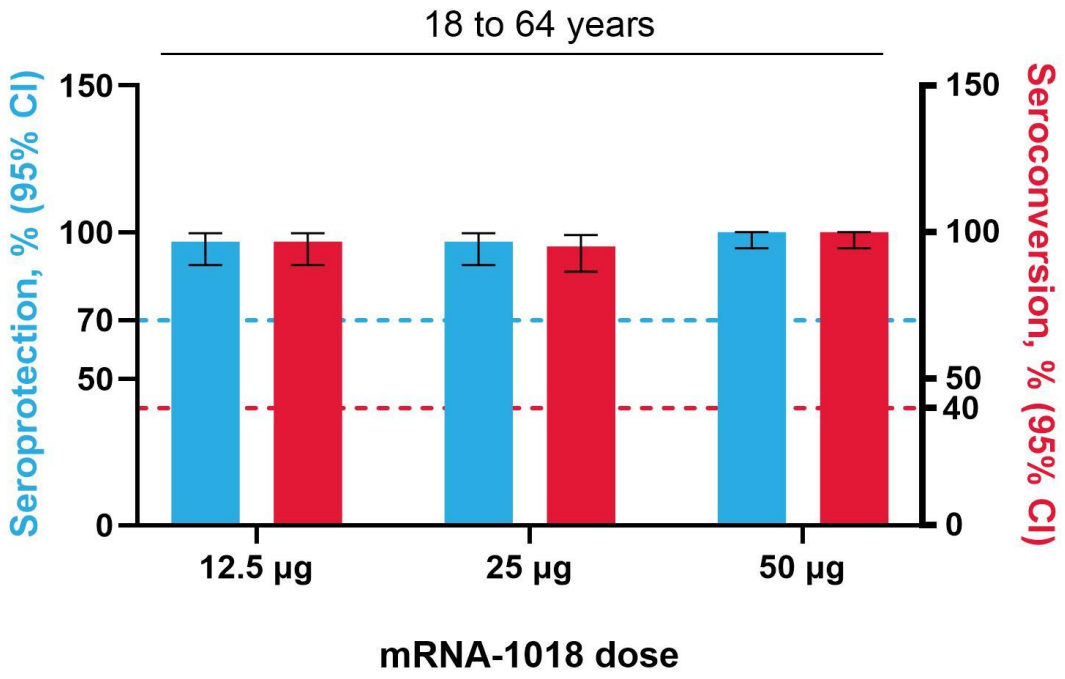
MN Titers in the Overall Population After Vaccination with mRNA-1018 (H5-CG)

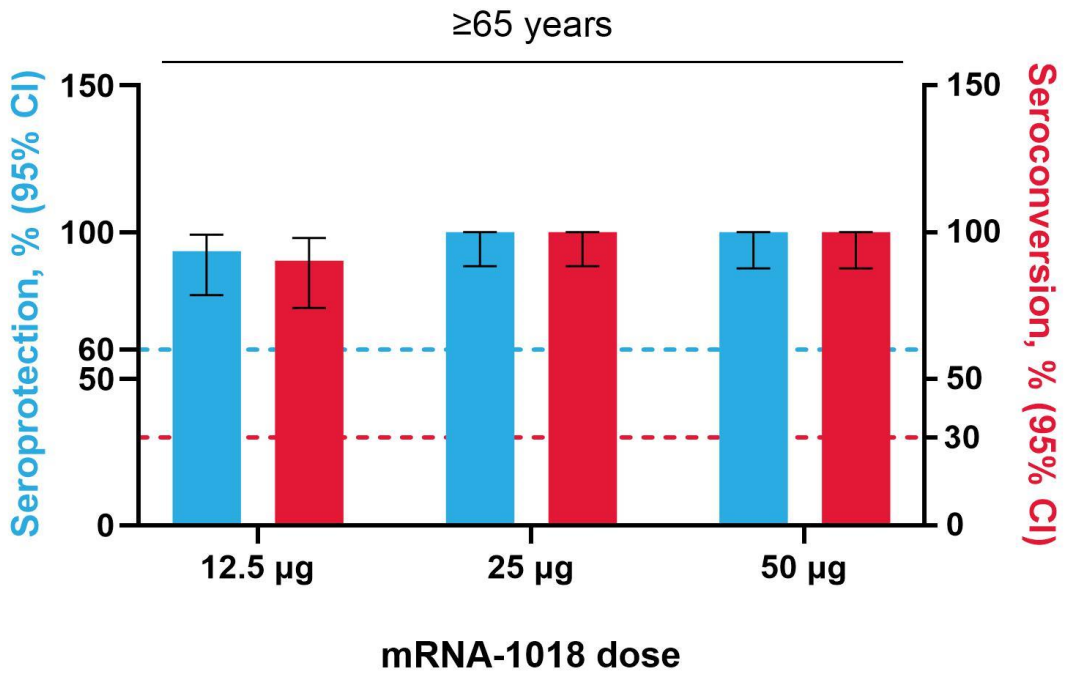


- MN responses were evident on Day 22, peaking on Days 29 and 43
- At Day 205, MN titers declined but remained above baseline
- The magnitude of the MN response increased with dose level, with the highest titers observed among participants who received the 50-µg dose

CI, confidence interval; CG, chicken Ghana; LLOQ, lower limit of quantification; MN, microneutralization; ULOQ, upper limit of quantification.
Per-protocol immunogenicity set. Overall: Baseline, n = 283; Day 8, n = 282; Day 22, n = 283; Day 29, n = 273; Day 43, n = 278; Day 205, n = 269.
Antibody values reported as below the LLOQ were replaced with 0.5 × LLOQ; values greater than the ULOQ wee converted to the ULOQ. LLOQ = 12; ULOQ = 558.9. Bars indicate MN titers with 95% CI. Dots correspond to participant-level titers.

Seroprotection and Seroconversion Rates After 2 doses of mRNA-1018 (H5-CG) by Age Cohort at Day 43





- Protective H5 HAI titers were observed following 2 doses of mRNA-1018
- At Day 43, the percentage of participants who received the 50 µg dose aged 18-64 years with HAI titers ≥1:40 was 100 % (95%CI 94.5,100), and 100% (87.7, 100) in participants aged ≥65 years
- At all dose levels, seroprotection and seroconversion rates met the CBER criteria, reaching the threshold for HAI titer ≥1:40 of at least 70% in adults aged 18 to <65 years, and at least 60% in adults aged ≥65 years after a single dose[1], and increasing substantially after the second dose

CI, confidence interval; CBER, Center for Biologics and Evaluation Research; CG, chicken Ghana; HAI, hemagglutination inhibition; SC, seroconversion; SP, seroprotection.
Per-protocol immunogenicity set. Aged 18 to 64 years: mRNA-1018 (12.5 µg), n = 62; mRNA-1018 (25 µg), n = 62; mRNA-1018 (50 µg), n = 65. Aged ≥65 years: mRNA-1018 (12.5 µg), n = 31; mRNA-1018 (25 µg), n = 30; mRNA-1018 (50 µg), n = 28.
HAI titers 1:40 titer associated with SP. Percentage of participants with SC was defined as titer ≥1:40 if baseline was <1:10 or a 4-fold or greater rise if baseline was ≥1:10 in HAI antibodies measured by the HAI assay. Error bars represent 95% CI. Blue and red dashed lines (HAI antibody titers ≥1:40 and seroconversion, respectively) indicate the CBER threshold clinical data needed to support licensure of influenza vaccines.[1]
1. Food and Drug Administration. Guidance for Industry. Clinical Data Needed to Support the Licensure of Seasonal Inactivated Influenza Vaccines. https://www.fda.gov/files/vaccines%2C%20blood%20%26%20biologics/published/Guidance-for-Industry--Clinical-Data-Needed-to-Support-the-Licensure-of-Seasonal-Inactivated-Influenza-Vaccines.pdf.

Conclusions

- **In this phase 1/2 trial, across all mRNA-1018 (H5-CG) doses evaluated, no tolerability or safety concerns were observed**
  - mRNA-1018 was generally well-tolerated across the range of doses tested
  - Most solicited ARs were grade 1 or 2 in severity; grade 3 solicited ARs were uncommon
- **mRNA-1018 induced strong functional and neutralizing immune responses across the range of doses tested**
  - HAI antibody responses ≥1:40, commonly associated with protection[1], were seen after 2 doses of mRNA-1018
  - Antibody responses were observed 7 days after a single dose, and persisted for 6 months after the second dose
  - The highest GMT, HAI titers ≥1:40, and seroconversion rates were observed with the 50-µg dose
- **mRNA-1018 demonstrated rapid and durable immune response of all doses tested across all adult age groups, which are considered key attributes of a pandemic vaccine**

AR, adverse reaction; CG, chicken Ghana; GMT, geometric mean titer; HAI, hemagglutination inhibition.
1. Kandinov et al. *Hum Vaccin Immunother.* 2025;21(1):2484088.

Thank you

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