SVF-7

Safety and Immunogenicity of a SARS-CoV-2 Spike Receptor-Binding and N-Terminal Domain COVID-19 Vaccine

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BACKGROUND

- mRNA-based vaccines protect against COVID-19[1]
- The original mRNA-1273 vaccine encodes for the full-length SARS-CoV-2 spike protein
- mRNA-1283 is an investigational vaccine designed to encode for the immuno-dominant receptor-binding domain (RBD) and N-terminal domain (NTD) of the spike protein
  - Shorter mRNA with the potential for enhanced thermostability
  - Elicits similar immune responses compared to mRNA-1273[2]

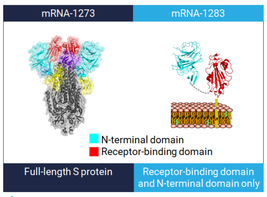


Figure 1. Encoded Proteins, mRNA-1273 and mRNA-1283

Figure adapted from Stewart-Jones GBE et al. *Sci Transl Med.* 2023;15(713):eadf4100. Reprinted with permission from AAAS.

OBJECTIVES

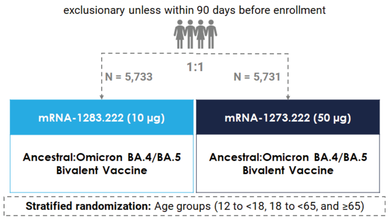
- Primary objectives were to assess non-inferior neutralizing antibody responses, non-inferior relative vaccine efficacy, and safety and reactogenicity of mRNA-1283.222 (10 µg) versus mRNA-1273.222 (50 µg)
- Interim safety and immunogenicity results are presented with a median follow-up of 3.25 months

METHODS

Study Design

- This poster summarizes interim findings from the mRNA-1283-P301: Booster Vaccine Safety, Immunogenicity, and Relative Vaccine Efficacy Study (NCT05815498), a randomized, observer-blind, active-controlled phase 3 trial (**Figure 2**)
- 11,464 individuals aged ≥12 years were assigned to receive either a single intramuscular injection of mRNA-1283.222 (10 µg) or mRNA-1273.222 (50 µg) at baseline (Day 1)
- Participant demographics and baseline characteristics were balanced between both groups (**Figure 3**)

Figure 2. Overview of Study Design



Immunogenicity Assessments

This poster presents neutralizing antibody responses against Omicron BA.4/BA.5 and Ancestral D614G at baseline and Day 29 for mRNA-1283.222 versus mRNA-1273.222

Safety Assessments

This poster presents:

- Solicited local and systemic adverse reactions (ARs) up to Day 7 after vaccination
- Unsolicited adverse events (AEs) up to Day 28 after vaccination
- Serious AEs up to Day 28 after vaccination

Figure 3. Participant Demographics and Baseline Characteristics Were Balanced Between Both Groups

Safety Set

	mRNA-1283.222 (10 µg) N = 5711	mRNA-1273.222 (50 µg) N=5716
Mean age, years (range)	51.5 (12, 96)	51.2 (12, 90)
Median age, years	56	55
Age subgroup, %		
12-18 years	8.7%	8.7%
18-65 years	62.7%	62.6%
≥65 years	28.6%	28.7%
Non-white race, %	17.4%	16.9%
Median interval between last dose before enrollment and study vaccination, months (Q1, Q3)	9.8 (7.6, 16.9)	9.8 (7.7, 16.8)
Prior SARS-CoV-2 Infection, %[a]	73.6%	74.6%

[a]Evidence of SARS-CoV-2 infection pre-study vaccination.

RESULTS

Neutralizing Antibody Responses

Per-Protocol Immunogenicity Sets

Figure 4. Neutralizing Antibody Responses Against Omicron BA.4/BA.5 Were Higher With mRNA-1283.222 Than mRNA-1273.222

	mRNA-1283.222 (10 µg) N = 623	mRNA-1273.222 (50 µg) N=567
Baseline (Day 1)		
GMC (95% CI)	356.1 (325.1, 390.1)	343 (309.9, 380.8)
Day 29		
CMC (95% CI)	2336.2 (2148.8, 2539.8)	1754.5 (1607.4, 1915.1)
GMFR (95% CI)	6.6 (6.0, 7.2)	5.1 (4.7, 5.6)
ANCOVA GMC (95% CI)[a]	2324.1 (2151.5, 2510.4)	1754.5 (1618.8, 1901.6)
GMR (95% CI)[a]	**1.3 (1.2, 1.5)**	
SRR, % (95% CI)[b]	79.8 (76.4, 82.9)	65.6 (61.5, 69.5)
SRR difference, % (95% CI)	**14.2 (9.1, 19.2)**	

Success Criteria Met **GMR noninferiority:** Lower 95% CI of GMR was >0.667 **SRR difference noninferiority:** Lower 95% of CI of SRR difference was >-10%

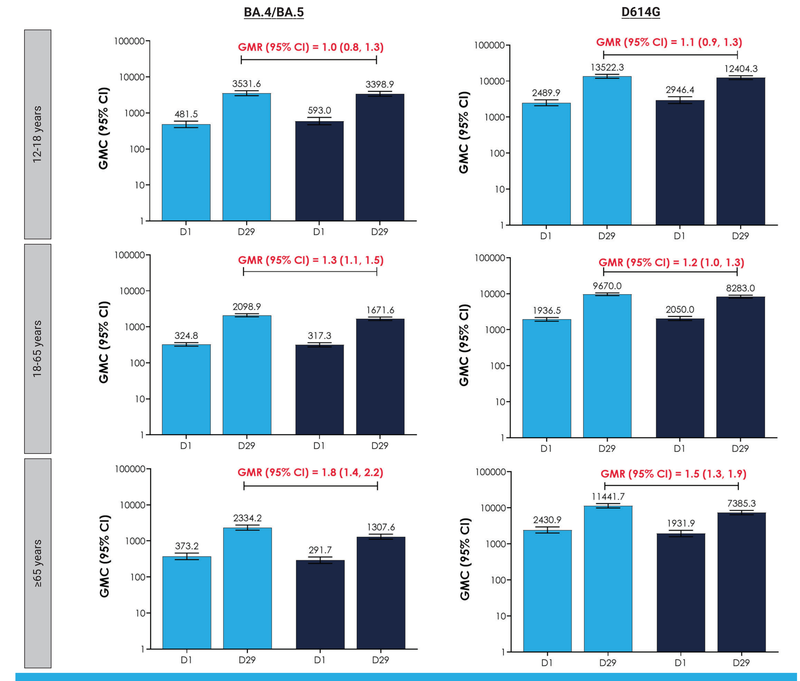
Figure 5. Neutralizing Antibody Responses Against Ancestral SARS-CoV-2 (D614G) Were Higher With mRNA-1283.222 Than mRNA-1273.222

	mRNA-1283.222 (10 µg) N = 623	mRNA-1273.222 (50 µg) N=567
Baseline (Day 1)		
GMC (95% CI)	2125.2 (1939.3, 2328.9)	2140.2 (1940.1, 2361.0)
Day 29		
CMC (95% CI)	10628.0 (9934.0, 11370.6)	8573.5 (7988.7, 9201.2)
GMFR (95% CI)	5.0 (4.6, 5.4)	4.0 (3.7, 4.4)
ANCOVA GMC (95% CI)[a]	10582.9 (9916.5, 11294.0)	8573.5 (8010.7, 9175.9)
GMR (95% CI)[a]	**1.2 (1.1, 1.4)**	
SRR, % (95% CI)[b]	83.6 (80.5, 86.4)	73.0 (69.2, 76.6)
SRR difference, % (95% CI)	**10.6 (6.0, 15.3)**	

Success Criteria Met **GMR noninferiority:** Lower 95% CI of GMR was >0.667 **SRR difference noninferiority:** Lower 95% of CI of SRR difference was >-10%

ANCOVA, analysis of covariance; CI, confidence interval; GMC, geometric mean concentration; GMFR, geometric mean fold rise; GMR, geometric mean ratio; LLOQ, lower limit of quantification; SRR, seroresponse rate.
[a]An ANCOVA model was carried out, with the dependent variable of the serum antibody value at Day 29 and the fixed variable of group (mRNA-1283.222 vs mRNA-1273.222) adjusted by SARS-CoV-2 status at pre-booster, age group, number of prior boosters, and type of primary series and prior booster vaccine, if applicable. Coefficients for Least Square Means use margins.
[b]Seroresponse at the participant level was defined as an antibody value change from baseline below the LLOQ to ≥4 × LLOQ; or ≥4-fold rise if baseline is ≥LLOQ and <4 × LLOQ; or ≥2-fold rise if baseline is ≥4 × LLOQ.

Figure 6. Higher Neutralizing Antibodies With mRNA-1283.222 Than mRNA-1273.222 Across Age Groups



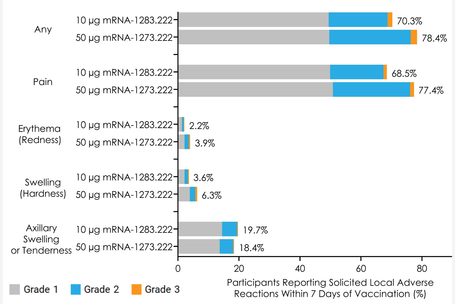
The highest neutralizing antibody GMR was observed in participants aged ≥65 years

CI, confidence interval; D, day; GMC, geometric mean concentration; GMR, geometric mean ratio.
12-18 years: mRNA-1283.222, N = 92; mRNA-1273.222, N = 93; 18-65 years: mRNA-1283.222, N = 378; mRNA-1273.222, N = 317; ≥65 years: mRNA-1283.222, N = 153; mRNA-1273.222, N = 157.

Safety

Figure 7. Solicited Local Adverse Reactions After mRNA-1283.222 Were Similar to mRNA-1273.222

Solicited Safety Set

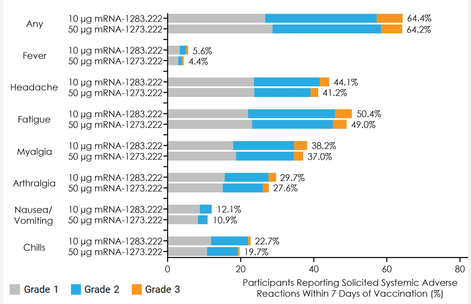


- Overall frequency of solicited local adverse reactions was 70.3%for mRNA-1283.222 and 78.4% for mRNA-1273.222
- Pain at the injection site was the most frequently observed solicited local adverse reaction for both groups

mRNA-1283.222, N = 5707; mRNA-1273.222, N = 5711.

Figure 8. Solicited Systemic Adverse Reactions After mRNA-1283.222 Were Similar to mRNA-1273.222

Solicited Safety Set



- Overall frequency of solicited systemic adverse reactions was 64.4% for mRNA-1283.222 and 64.2% for mRNA-1273.222
- Fatigue, headache, and myalgia were the most frequently observed solicited systemic adverse reactions for both groups

mRNA-1283.222, N = 5707; mRNA-1273.222, N = 5711. One participant in the mRNA-1273.222 group had a grade 4 fever.

mRNA-1283.222 Had a Similar Safety Profile to mRNA-1273.222

Safety Set; Up to 28 Days After Vaccination

- Adverse events were reported at similar rates between vaccine groups:
  - mRNA-1283.222: 11.5% (695/5711)
  - mRNA-1273.222: 11.2% (643/5716)
- Serious adverse events were reported at similar rates between- vaccine groups:
  - mRNA-1283.222: 0.2% (13/5711)
  - mRNA-1273.222: 0.3% (18/5716)

Summary

Immunogenicity

- Pre-specified primary immunogenicity objective was met
  - Neutralizing antibody responses were higher with mRNA-1283.222 vs mRNA-1273.222 (BA.4/BA.5 and D614G)
  - Neutralizing antibody responses were consistently higher with mRNA-1283.222 vs mRNA-1273.222 across all age groups
    - Highest GMR was observed in participants aged ≥65 years

Safety

- Local and systemic reactogenicity of mRNA-1283.222 was similar to mRNA-1273.222
- Safety profile of mRNA-1283.222 was similar to mRNA-1273.222

GMR, geometric mean ratio.

CONCLUSIONS

The SARS-CoV-2 spike RBD-NTD vaccine elicited higher neutralizing antibody responses than the original, full-length-spike vaccine. The frequency of reactogenicity and adverse events was similar between the vaccines and no safety concerns were identified for mRNA-1283.222.

References

1. Baden LR et al. *N Engl J Med.* 2021;384(5):403-416.
2. Stewart-Jones GBE et al. *Sci Transl Med.* 2023;15(713):eadf4100.

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ADDITIONAL INFORMATION

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