Immunogenicity and Safety of a Virus-Like Particle (VLP) Protein Subunit SARS-CoV-2 Vaccine in Adults: A Phase 1/2 Study

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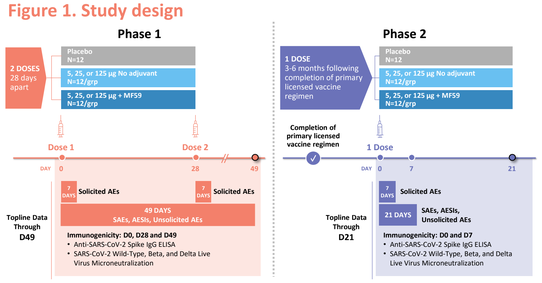
INTRODUCTION

- More than two years after the start of the pandemic, COVID-19 continues to cause substantial morbidity and mortality worldwide
- Continued vaccination of groups at high-risk of severe COVID-19 is likely to be needed in future years to boost immunity
- Virus-like particle (VLP) vaccines mimic the structure of real viruses, potentially resulting in a superior immune response compared with soluble antigens
- In this phase 1/2 study, we evaluated the immunogenicity and safety of a VLP protein subunit SARS-CoV-2 vaccine (IVX-411) with or without Seqirus Inc.'s proprietary squalene-based oil-in-water emulsion adjuvant MF59® (MF59) in adults aged 18–69

METHODS

- Phase 1 included 84 SARS-CoV-2-naïve subjects whereas Phase 2 included 84 previously vaccinated subjects*

Figure 1. Study design



* Received either Pfizer or Astra Zeneca vaccine.

- Primary endpoints
  - Solicited (to Day 7) and unsolicited adverse events (AEs)
  - Neutralizing antibody (Ab) titers
  - Spike protein-specific IgG Ab titers
- Other endpoints (ongoing)
  - Serious AEs (SAEs), medically-attended AEs (MAAEs), AEs of special interest (AESIs), and AEs leading to study withdrawal up to Day 210
  - Immunogenicity up to Day 210

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RESULTS

DEMOGRAPHICS

- Demographics were similar between the IVX-411 and placebo groups in both study phases

SAFETY

- Local reactogenicity was mild-to-moderate and higher with increased doses or addition of adjuvant (Figure 2); rates of systemic AEs were similar to placebo in both phases (Figure 3)
- No AESIs or AEs leading to study withdrawal were reported
- Four SAEs were reported, none were considered related to vaccination and all began after Day 21 following vaccination
- Unsolicited AEs were mostly mild and rates were similar to placebo in both phases

Figure 2. Local AEs within 7 days of any dose

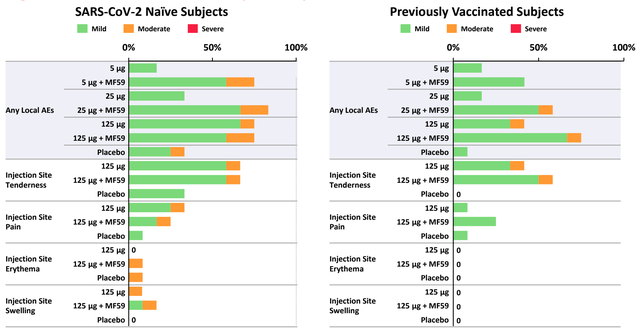
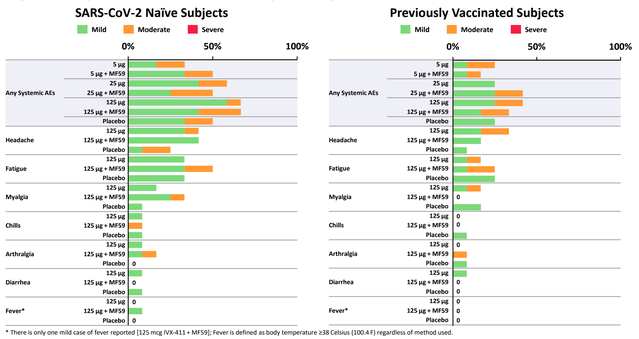


Figure 3. Systemic AEs within 7 days of any dose

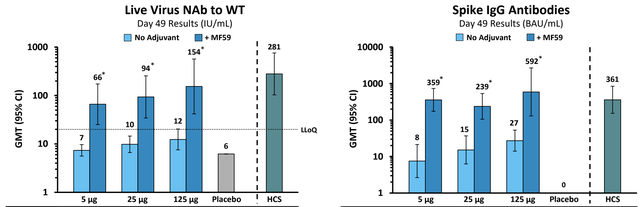


* There is only one mild case of fever reported [125 mcg IVX-411 + MF59]; Fever is defined as body temperature ≥38 Celsius (100.4 F) regardless of method used.

IMMUNOGENICITY

- A limited dose-effect was seen in SARS-CoV-2-naïve subjects, with significantly higher antibody titers in the groups receiving adjuvant. Across groups, titers were similar or lower than human convalescent sera (Figure 4)
- No clear dose or adjuvant effect was seen in previously vaccinated subjects, with titers rising from baseline levels across all dose/adjuvant combinations (Figure 5)

Figure 4. Neutralizing and spike IgG Abs in SARS-CoV-2-naïve subjects



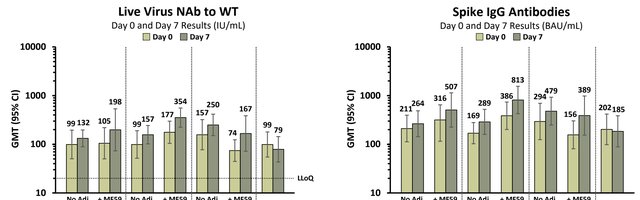
	5 µg		25 µg		125 µg		Placebo	HCS
N=	12	12	12	12	12	11	11	10
Fold-rise vs HCS	0.02	0.23	0.04	0.33	0.04	0.55	0.02	-
Fold-rise vs BL	1.2	10.7	1.6	15.1	2.0	20.9	1.0	-
Seroresponse Rate	0	58.3	0	75.0	16.7	58.3	0	-

*p < 0.01 vs. no adjuvant.

	5 µg		25 µg		125 µg		Placebo	HCS
N=	12	12	12	12	12	11	11	10
Fold-rise vs HCS	0.02	0.99	0.04	0.66	0.07	1.64	0.00	-
Fold-rise vs BL	21	884	54	537	60	1466	1	-
Seroresponse Rate	83.3	100	91.7	100	91.7	100	0	-

*p < 0.01 vs. no adjuvant.

Figure 5. Neutralizing and spike IgG Abs in previously vaccinated subjects

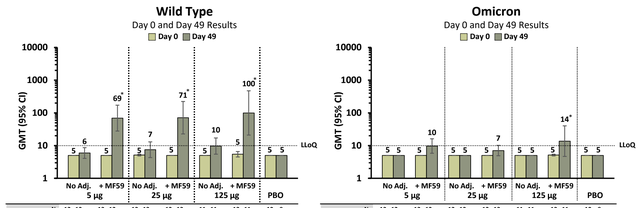


	No Adj. 5 µg		+ MF59 5 µg		No Adj. 25 µg		+ MF59 25 µg		No Adj. 125 µg		+ MF59 125 µg		PBO	
N=	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Fold-rise vs BL	1.3		1.9		1.6		2.0		1.6		2.2		0.8	
Seroresponse Rate	16.7		33.3		25.0		33.3		25.0		33.3		0	

	No Adj. 5 µg		+ MF59 5 µg		No Adj. 25 µg		+ MF59 25 µg		No Adj. 125 µg		+ MF59 125 µg		PBO	
N=	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Fold-rise vs BL	1.3		1.6		1.7		2.1		1.6		2.5		0.9	
Seroresponse Rate	0		8.3		0		8.3		8.3		33.3		0	

- Similar findings were observed across tested variants of concern (beta, delta, and omicron), with up to 7-fold rises from baseline titers against omicron (Figures 6 and 7)

Figure 6. Neutralizing Ab titers against wild type and omicron – SARS-CoV-2-naïve



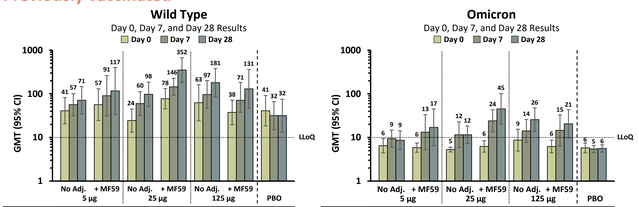
	No Adj. 5 µg		+ MF59 5 µg		No Adj. 25 µg		+ MF59 25 µg		No Adj. 125 µg		+ MF59 125 µg		PBO	
N=	12	12	12	12	12	12	12	12	11	11	12	11	10	9
Fold-rise vs BL	1		14		2		14		2		18		1	
Seroresponse Rate	8		75		17		58		9		73		0	

*p < 0.01 vs. no adjuvant.

	No Adj. 5 µg		+ MF59 5 µg		No Adj. 25 µg		+ MF59 25 µg		No Adj. 125 µg		+ MF59 125 µg		PBO	
N=	12	12	12	12	12	12	12	12	11	11	12	11	10	9
Fold-rise vs BL	1		2		1		5		1		3		1	
Seroresponse Rate	0		8		0		0		0		27		0	

*p < 0.01 vs. no adjuvant.

Figure 7. Neutralizing Ab titers against wild type and omicron – Previously vaccinated



	No Adj. 5 µg			+ MF59 5 µg			No Adj. 25 µg			+ MF59 25 µg			No Adj. 125 µg			+ MF59 125 µg			PBO		
N=	12	12	12	10	11	11	12	12	12	11	11	11	10	11	11	11	12	12	12	12	12
Fold-rise vs BL*	1	2		2	2		2	4		2	5		1	3		2	4		1	1	
Seroresponse Rate	0	30.0		25.0	9.1		10.0	18.2		0	0		0	0		0	0		0	0	

	No Adj. 5 µg			+ MF59 5 µg			No Adj. 25 µg			+ MF59 25 µg			No Adj. 125 µg			+ MF59 125 µg			PBO		
N=	12	12	12	11	11	11	12	12	12	11	11	11	10	11	11	11	12	12	12	12	12
Fold-rise vs BL*	1	1		2	3		2	2		4	7		3	3		2	3		1	1	
Seroresponse Rate	0	27.3		16.7	27.3		10.0	27.3		0	0		0	0		0	0		0	0	

CONCLUSIONS

- The vaccine demonstrated acceptable tolerability profiles in SARS-CoV-2-naïve and previously vaccinated subjects
- Immunogenicity was observed in both primary and booster vaccination, with a clear adjuvant effect in SARS-CoV-2-naïve subjects
- Immune responses were seen across variants of concern in both study phases
- Immunogenicity was lower than expected based on previous studies – further investigations showed this to be due to antigen instability in the receptor binding domain and unique to this vaccine candidate
- Future plans include evolution of antigen design for incorporation into a potential bivalent COVID-19 candidate vaccine and other combination VLP vaccines