SAFETY OF HETEROLOGOUS MRNA-1273 BOOST AFTER AD26.COV2.S PRIME IN SOUTH AFRICA

1012

Nigel Garrett[1,2§], Ameena Goga[3,4], Tarylee Reddy[3], Azwidhwi Takalani[5], Kubashni Woeber[3], Phumeza Jonas[5], Imke Engelbrecht[6], Ishen Seocharan[3], Jacqueline Odhiambo[5], Kentse Khuto[5], Nonhlanhla Yende-Zuma[1], Kate Anteyi[7], Brett Leav[7], Linda Gail Bekker[8, 9], Glenda E Gray[3] and the SHERPA study team

1. Centre for the AIDS Programme of Research in South Africa (CAPRISA), South Africa; 2. Discipline of Public Health Medicine, University of KwaZulu-Natal, SA; 3. South African Medical Research Council, SA; 4. University of Pretoria, SA; 5. Vaccine and Infectious Diseases Division, Fred Hutch Cancer Research Center, Seattle, WA, US; 6. Right to Care, SA; 7. Moderna, Inc, Cambridge, MA, United States; 8. Desmond Tutu Health Centre, University of Cape Town, SA. 9. University of Cape Town, SA

BACKGROUND

- There is a paucity of data on safety and effectiveness of mRNA COVID-19 booster vaccinations in lower income settings with high HIV prevalence.
- We evaluated a heterologous mRNA-1273 (Moderna) boost after priming with 1 or 2 doses of Ad26.COV2.S (Janssen/ Johnson & Johnson) vaccine among health care workers (HCWs) in South Africa.

METHODS

- SHERPA (Sisonke Heterologous mRNA-1273 boost after prime with Ad26.COV2.S) is an open-label, phase 3 mRNA-1273 booster study, nested in the Sisonke Phase 3b implementation trial, that vaccinated ~500,000 HCWs with 1 or 2 doses of Ad26.COV2.S from Feb - Dec 2021.
- Sisonke participants were offered mRNA-1273 boosters at 30 clinical research sites across South Africa between 23 May and 12 Nov 2022, a median (IQR) of 17 (16 - 18) and 8 (7 - 10) months after 1 or 2 doses of Ad26.COV2.S vaccination, respectively
- Data was cut off on 12 Dec 2022.
- Reactogenicity and adverse events (AEs) were self-reported via an online data entry link shared by SMS with participants 1, 7 and 28 days after boosting.
- We used multivariable logistic regression models to assess variables associated with reactogenicity events.

Table 1: Study schema of Sisonke mRNA-1273 boost and comparator groups

Study Groups	Sisonke (Feb–May 2021)	Sisonke 2 (Nov-Dec 2021)	mRNA boost (SHERPA May-Nov 2022)
mRNA boost Group 1	Ad26.COV2.S	Ad26.COV2.S	mRNA-1273
mRNA boost Group 2	Ad26.COV2.S	X	mRNA-1273
Sisonke Comparator Group 1	Ad26.COV2.S	Ad26.COV2.S	X
Sisonke Comparator Group 2	Ad26.COV2.S	X	X

A mRNA-1273 booster vaccine administered after 1 or 2 doses of Ad26.COV2.S was well tolerated regardless of HIV status, other chronic conditions or prior SARS-CoV-2 infection status in South Africa.

RESULTS

- 12188 HCWs (79.5% female, 28.6% with self-reported previous SARS-CoV-2 diagnosis) received a mRNA-1273 booster, of whom 44.6% had received 1 prior dose and 55.4% 2 prior doses of Ad26.COV2.S vaccines in Sisonke (**Table 1**).
- 3056 (25.2%) reported being HIV positive, more among those receiving only 1 versus 2 previous Ad26.COV2.S (26.8% vs 23.9%). Of these, 1.4% reported not being on antiretroviral therapy. 17.0% of participants reported hypertension and 6.4% diabetes mellitus.
- 262/12188 participants (2.1% of women, 2.5% of men) reported 234 reactogenicity events and 95 AEs post-vaccination. More events were reported by participants with prior SARS-CoV-2 infection (3.5% vs 1.6%), HIV negative status (2.5% vs 1.2%) and those who received 2 prior doses of Ad26.COV2.S compared to 1 dose (2.4% vs 1.8%) (**Table 2**).

Table 2: Multivariable logistic regression model of local/systemic reactions adjusted for age and gender

	n (%) reporting AE/reactogenicity	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Prior COVID diagnosis			
No	141/ 8696 (1.6%)	Reference	
Yes	121/ 3486 (3.5%)	2.18 (1.70 - 2.79)	2.15 (1.68 - 2.76)
HIV status			
No	224/ 9056 (2.5%)	Reference	
Yes	38/ 3056 (1.2%)	0.50 (0.35 - 0.70)	0.54 (0.38 - 0.77)
Prior vaccination			
1 Ad26.COV2.S	100/ 5437 (1.8%)	Reference	
2 Ad26.COV2.S	162/ 6751 (2.4%)	1.31 (1.02 - 1.69)	1.32 (1.02 - 1.70)

RESULTS cont.

- Among 159 (1.3%) reporting injection site reactions the commonest were pain (59.7%), swelling (42.1%) and induration (20.1%).
- Of 177 (1.5%) systemic reactogenicity events (all grade 1 or 2 severity), the commonest were myalgia (69.5%), headache (67.8%) and fever (37.9%).
- 14 participants had AEs of special interest or serious AEs, of which 4 (all grade 1 AESIs of ageusia or anosmia) were deemed related to the mRNA-1273 booster. There were 2 death, unrelated to study product.
- Of 64 confirmed pregnancies, 1 AE of gestational diabetes was reported, unrelated to study product.
- 13 COVID-19 infections occurred a median of 125 days post booster vaccination (IQR 90–154) after 3477 person-years of follow up.

CONCLUSIONS

- A mRNA-1273 booster administered after 1 or 2 doses of Ad26.COV2.S was well tolerated regardless of HIV status, other chronic conditions or prior SARS-CoV-2 infection status.
- Analyses are underway to compare mRNA-1273 booster effectiveness against SARS-CoV-2 infections and severe COVID-19 with Sisonke participants who did not receive the booster.

ADDITIONAL KEY INFORMATION

Funding: The study was sponsored by the South African Medical Research Council and funded by Moderna, Inc. The vaccine product was provided by Moderna, Inc. The study was approved by the South African Health Products Regulatory Authority (SAHPRA) and ethics committees of participating clinical research sites

§ **Corresponding author**: nigel.garrett@caprisa.org

Acknowledgements: We thank the participants, the protocol and safety teams, the site-Principal Investigators and their teams, SAHPRA, and the ethics committees for their contribution and oversight of the study.