

CHALLENGES IN ASSESSING IMMUNE RESPONSES AFTER SARS-CoV-2 VACCINATION

Dr PR Vermaak^a, Dr S Mayaphi^a

^aDepartment of Medical Virology, University of Pretoria / Tshwane Academic Division of NHLS, South Africa

Introduction

- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has resulted in an ongoing global pandemic
- Over 207 million cases and more than 4.3 million deaths
- Over 4.6 billion vaccine doses administered
- 3 958 231 people vaccinated in South Africa as of 16 August 2021
- This report describes a case of apparent primary coronavirus disease (COVID-19) vaccine failure as part of the Sisonke study phase 3B Janssen COVID-19 vaccine rollout in South Africa

Case Description

- 72 year old male
- No known co-morbidities
- Received Johnson & Johnson COVID-19 vaccine 22/02/2021
 - Antibody test done at private laboratory in JHB
 - EUROIMMUN Anti-SARS-CoV-2 (S protein IgG)
 - No demonstrable antibody response
- Retested day 32 post-vaccination
 - Same assay
 - No demonstrable antibody response
- T-cell responses then measured (same day)
 - In-house T-cell lymphocyte proliferation test utilising flow cytometry
 - Positive result attained

Immune responses

- Immune responses (NEJM: interim results of phase 1-2a trial)
 - Neutralizing-antibody titers against wild-type virus detected in >90% of all participants on day 29
 - 96% by day 57
 - CD4+ T-cell responses were detected in 76-83% of the participants 18-55 years, 60-67% >65 years
 - Robust CD8 T-cell responses

Antibody Testing

- IgG and/ or IgM may be measured to spike and/or nucleocapsid protein of SARS-CoV-2
 - Measures humoral response
- Various laboratory assays have varying sensitivities and specificities
- A negative antibody test may mean:
 - No infection with SARS-CoV-2 (or vaccination)
 - No antibodies developed
 - Immunodeficiency
 - Extremes of age
 - Other co-morbidities
 - Genetic factors
 - False negative result
 - Testing too early
 - Fluctuation in antibody levels
 - Assay limitations
- Most commercially available antibody assays measure antibodies to nucleocapsid protein
 - Not seen in vaccinated patients as the vaccine is based on the spike protein
 - Do not measure cellular immune responses

Vaccine

- The Janssen vaccine candidate is a recombinant, replication-incompetent adenovirus serotype 26 vector
- Mechanism of action
 - Vector: Adenovirus 26 with E1 gene deletion- renders virus replication incompetent
 - Transgene added that encodes for SARS-CoV-2 spike protein (not entire virus)
 - Administered via IM injection
 - Enters the cells and instructs the cell machinery to produce spike protein found on the surface of SARS-CoV-2 (not virus)
 - Cells display spike protein on their surface- triggers immune response
- Ad26-based vaccines well tolerated
- No significant safety issues identified
- Strong, durable humoral and cellular responses demonstrated
- Effect of pre-existing immunity to Ad26 not yet shown to have an impact on vaccine immunogenicity
- Efficacy (28 days after inoculation)
 - 85.4% against severe disease and hospitalization
 - 66.9% against symptomatic moderate and severe infection

Conclusion

- In the public sector, available assays that only detect SARS-CoV-2 spike protein or nucleocapsid protein antibodies may not be adequate for assessing post-vaccination immune response
- Cell mediated responses also represent part of the vaccination response
- False impression of vaccine failure in vaccinated individuals with negative antibody tests post-vaccination
- Antibody testing not currently recommended for assessing immune responses to vaccination for SARS-CoV-2
- Currently no recommendations regarding re-vaccination
- More data and research needed

References

1. The J&J covid-19 vaccine: What you need to know. World Health Organisation; 2021. Sadoff J, Le Gars M, Shukarev G, Heerwegh D, Truyers C, de Groot AM, et al.
2. Interim results of a phase 1-2a trial of ad26.Cov2.S covid-19 vaccine. New England Journal of Medicine. 2021; 384(19):1824-35. doi:10.1056/NEJMoa2034201
3. [Internet]. Covid-19 dashboard. Johns Hopkins University of Medicine; 2021 [cited 2021 24 June 2021]. Available from: <https://coronavirus.jhu.edu/map.html>.