COVID-19 vaccines: are we good to go?

The COVID-19 pandemic has accelerated unprecedented research of experimental treatments as well as using established drugs in new ways. At the end of November 2020, we reflected on the various therapies for COVID-19 that had received regulatory full or emergency use authorisation including the convalescent plasma-derived IgG1 antibodies, bamlanivimab, and the casirivimab-imdevimab cocktail, that provide passive immunity in patients with mild to moderate disease who are at risk for severe illness, the intravenous antiviral, remdesivir, for patients with severe disease requiring hospitalisation, as well as the WHO-endorsed systemic inexpensive glucocorticoids such as dexamethasone, hydrocortisone, methylprednisolone or prednisone for critically ill patients requiring oxygen.1

More recently in the UK, doctors are encouraged to administer one of the repurposed rheumatoid arthritis interleukin-6 receptor antagonists, tocilizumab or sarilumab, to any COVID-19 patient who, despite receiving dexamethasone, is deteriorating and needs intensive care.2 Preliminary interim results of the REMAP-CAP trial have shown that these anti-inflammatory drugs may reduce fatality by almost a quarter compared to standard care, and allow patients to leave ICU an average of 7–10 days earlier.3-6 On the 28th of January, SAHPRA granted section 21 authorisation to ivermectin, allowing controlled compassionate access to this anti-parasitic drug in South Africa.

Regarding future therapies, clinical trials of inhaled nebulised interferon-β 1a, the cytokine that is the primary driver of the lung’s innate immune response, are on-going and initial results appear promising.7 It is purported that at-risk patients with comorbidities, older people, and recipients of immunosuppressive medication, produce less interferon-β, which contributes to their risk of more severe lung disease.

The best weapon against a virus though, is an effective and safe vaccine. Nearing the end of last year, we were super-excited about the first-of-its-kind, two-dose, Pfizer-BioNTech mRNA vaccine that showed 95% efficacy. This vaccine was approved by UK regulators less than a month after these reports, and outside of the clinical trial setting, was first administered on 8 December 2020 to Margaret Keenan, a 91-year-old who was in a Coventry hospital for cardiac investigations. By all accounts, she fared well. Other notable recipients include Dr Anthony Fauci, HRH Queen Elizabeth II, President-elect Joe Biden, Kamala Harris, Pope Francis, care home residents and hundreds of thousands of frontline healthcare workers. The most vulnerable are receiving COVID-19 vaccines in Europe, USA, South America, India, China and Russia, amongst others. In the UK alone, an estimated 10 million vaccine doses have been administered to date. However, no one has received a COVID-19 vaccine in South Africa.

We feel the urgency because our COVID-19 patient numbers, hospitalisations and deaths have soared, placing our healthcare systems and resolve under enormous pressure. The new South African fast-spreading SARS-CoV-2 501Y.V2 variant has caused pandemonium.3 Pfizer-BioNTech have reassured us that their mRNA vaccine is effective against not only the UK’s highly contagious variant, B.1.1.7, which carries eight changes to the spike protein receptor-binding domain, but also against the South African, which carries nine.8,9 Interestingly, the E484K mutation in the South African variant, as well as the N-terminal domain mutation in both the South African and the UK variants, have been found to escape recognition by neutralising antibodies generated in response to infection in vitro, implying that human antibody responses may be directed against a very small or different part of the virus’s spike protein or that other arms of the immune system may be triggered by these mRNA vaccines.10-11 Pfizer-BioNTech’s preservative-free mRNA vaccine (30 µg, 0.3 ml each; 2 intramuscular doses, 21 days apart) may be a bit tricky in our setting as it requires expensive minus 70 °C storage facilities, and this freezing cold chain needs to be maintained. It is supplied in a multi-dose vial containing 6 doses. The vaccine is intended for recipients aged 16 years or over.

Modernon’s 94% effective mRNA vaccine is based on similar technology: human ribosomes use the artificial mRNA to build components of the viral spike protein, which acts as an antigen that elicits immune responses.12 The Massachusetts-based biotech company recently reported that its vaccine is also effective against the UK and South African variants, but disappointingly, neutralising antibody efficacy is somewhat reduced for the latter.13 SARS-CoV-2 re-infection by variants is a realistic threat. The advantage of Modernon’s mRNA vaccine (100 µg, 0.5 ml; 2 intramuscular doses, 28 days apart), is that it may be stored at -20 °C (range -25 °C to -15 °C), and may be refrigerated between 2 °C and 8 °C for up to 30 days before vials are punctured. This vaccine is licensed for adults from 18 years of age. There is no maximum interval between the first and second doses for either of these mRNA vaccines, and this may justify delaying the second dose to 12 weeks in order to double the initial vaccination efforts in healthcare workers and the vulnerable. These products are not interchangeable.14 The CDC recommends that vaccination should be offered to persons regardless of a history of prior symptomatic or asymptomatic
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and dealing remind us that "In love we find out who we want to
be, in war we find out who we really are!" The ambitious aim is
to vaccinate two thirds of the South African population by the
end of the year. Our budget is R30 billion. The rollout is fraught
with logistical challenges requiring fine negotiations. Will the pi-
oneering plan to distribute COVID vaccines equitably succeed?

The race is on: we are aware that the population should be
vaccinated before the virus mutates irrevocably, particularly in
its spike protein and receptor binding region. Demand for the
vaccines is high, supply is low. Countries are scrambling to fulfil
their obligations to their citizens and manufacturers are under
enormous pressure. The unscrupulous and frantic wheeling
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The COVAX project aimed to pool the purchasing power of international funders to buy sufficient vaccine to immunise
20% of the most vulnerable globally. High- and middle-income
countries would receive a share of the vaccine in return for their
money, while lower income countries would receive vaccines
free of charge. Higher-funding countries though, appear to be
securing current and future vaccine doses directly from suppli-
ers, potentially leaving insufficient supply for poorer countries.
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We fear that we may receive too little, too late, thus driving local
and therefore global viral transmission.

The good news is that on 14 January, the African Union procured
270 million doses of COVID-19 vaccines from Pfizer, AstraZeneca,
and Johnson & Johnson to supplement the COVAX programme.
These should be available for the so-called critical periods of
April through June. However, the Johnson & Johnson one-shot
vaccine, also a recombinant, replication-incompetent adenovirus
serotype 26 vector, encoding a full-length and stabilised SARS-
CoV-2 spike protein, is still seeking regulatory approval. Results released at the end of January showed an overall 66% efficacy
in preventing moderate to severe disease (57% in South Africa),
and an 85% efficacy in preventing severe. This vaccine can be
refrigerated for months, which simplifies the logistics of
vaccinating large and rural groups of people. Production is
yet to be ramped up, but in time, South Africa is set to acquire
nine million doses of this vaccine. That potentially leaves us with
a shortfall, considering that two doses of vaccines are usually
required and that we are aiming to inoculate 40 million people
this year.

Are we good to go? The effectiveness and safety of these
vaccines are our chief concerns, but we have numerous
hurdles to overcome. Additional rollout considerations include manufacture, price, procurement, import, storage
and distribution infrastructures, community vaccination pro-
grames, acceptance of vaccines, and acquiring data on the
duration of vaccine effect, whether viral transmission is also
reduced, mutating viruses, and efficacy in vulnerable groups
including the elderly and those with comorbidities. Because
supplies, capabilities and capacities are limited, vaccines will
initially be allocated to frontline healthcare workers (1.2 million),
then to essential workers, the over 60s, and the over 18s with
comorbidities (18 million), and finally to the remaining over 18s
(22.5 million). All healthcare workers who wish to be vaccinated
should register on the central electronic vaccine data system
(EVDS). An appointment will then be sent by SMS. There is talk
that South Africa is prepared to act quickly, riding on the back of
large HIV rollout programmes. Time will tell if these platforms are
successful. In the meantime, we simply must continue to wash
our hands, sanitise, wear face masks and other PPE, maintain
physical distance, and shield, quarantine or isolate if necessary,
in order to dampen the terrible effects of this nasty little virus.

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References
1. Outhoff K. COVID-19 treatment: a growing (anti) body of evidence. South African General Practitioners Journal. 2020;15(1):172-4.
2. NHS patients to receive life-saving COVID-19 treatments that could cut hospital time by 10 days. Available from: https://www.gov.uk/government/news/nhs-patients-to-receive-life-saving-covid-19-treatments-that-could-cut-hospital-time-by-10-days#:~:text=wellbeing%20during%20coronavirus-,NHS%20patients%20to%20receive%20life%20saving%20COVID%20treatments%20that%20could%20cut%20hospital%20time%20by%2010%20days.-Accessed%208%20January%202021.
3. Stone JH, Frigault MJ, Serling-Boyd NJ, et al. Efficacy of tocilizumab in patients hospitalized with Covid-19. N Engl J Med. 2020;383(24):2333-44. https://doi.org/10.1056/NEJMoa2028836.
4. Gueradil G, Meschali M, Cozzi-Lepri M, et al. Tocilizumab in patients with severe COVID-19: a retrospective cohort study. The Lancet Rheumatology. 2020;2(8):e474-e84. https://doi.org/10.1016%2FS2665-9913(20)30173-9.
5. Della-Torre E, Campochiaro C, Cavalli G, et al. Interleukin-6 blockade with sarilumab in severe COVID-19 pneumonia with systemic hyperinflammation: an open-label cohort study. Ann Rheum Dis.
2020;79(10):1277-85. https://doi.org/10.1136/annrheumdis-2020-218122.

6. Gordon AC, Mouncey PR, Al-Beidh F, et al. Interleukin-6 receptor antagonists in critically ill patients with Covid-19 – Preliminary report. medRxiv. 2021;2021.01.07.21249390.

7. Monk PD, Marsden RJ, Tear VJ, et al. Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial. The Lancet Respiratory Medicine. 2020. https://doi.org/10.1016/S2213-2600(20)30511-7.

8. Tegally H, Wilkinson E, Giovanetti M, et al. Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa. medRxiv. 2020.2020.12.21.20248640. https://doi.org/10.1101/2020.12.21.20248640.

9. Xie X, Zou J, Fontes-Garfias CR, et al. Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera. bioRxiv. 2021;2021.01.07.425740. https://doi.org/10.1101/2021.01.07.425740.

10. Andreano E, Piccini G, Licastro D, et al. SARS-CoV-2 escape in vitro from a highly neutralizing COVID-19 convalescent plasma. bioRxiv. 2020;2020.12.28.244451. https://doi.org/10.1101/2020.12.28.244451.

11. Greane AJ, Loes AN, Crawford KHD, et al. Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies. bioRxiv. 2021;2021.12.31.425021. https://doi.org/10.1101/2021.12.31.425021.

12. Mahase E. Covid-19: Moderna vaccine is nearly 95% effective, trial involving high risk and elderly people shows. BMJ. 2020;371:m4471. https://doi.org/10.1136/bmj.m4471.

13. Wu K, Werner AP, Molivi J, et al. mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. https://doi.org/10.1101/2021.01.25.427948.

14. Centers for Disease Control and Prevention (CDC). COVID-19 vaccination: Clinical resources for each COVID-19 vaccine. Available from: https://www.cdc.gov/vaccines/covid-19/index.html. Accessed 10 January 2021.

15. Castells MC, Phillips EJ. Maintaining safety with SARS-CoV-2 vaccines. N Engl J Med. 2020. https://doi.org/10.1056/NEJMra2035343.

16. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. The Lancet. 2021;397: 99-111. https://doi.org/10.1016/S0140-6736(20)32661-1.

17. Health on SAHPRA commencing review of vaccine application for registration for Coronavirus Covid-19. Available from: https://www.gov.za/speeches/health-sahpra-commencing-review-vaccine-application-registration-coronavirus-covid-19-15. Accessed 10 January 2021.