Title: Vaccine Dividend following One Dose of the COVID-19 Vaccine Vaxzevria®

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Action required:
☐ For noting
☐ For discussion
x For decision

Approved for future publication: NO
Introduction

COVID-19 vaccines licensed by the European Medicines Agency (EMA) have been shown during clinical trials to be highly effective in providing protection against symptomatic and severe COVID-19. Moreover, real-world evidence in respect of the use of these vaccines has established high vaccine effectiveness against PCR-confirmed SARS-CoV-2 infection. The Centres for Disease Control (CDC) and the EMA have both recently published interim guidance with respect to the benefits of full vaccination.

In recognition of the (i) decreased risk of developing serious disease once fully vaccinated, and the (ii) the importance of a vaccine dividend in maintaining momentum in the ongoing roll-out of the vaccination programme, a series of measures have been introduced over the past month in relation to those who had completed their full vaccine regimen. The HSE/HPSC has produced public health guidance to facilitate safe indoor visits between vaccinated persons and to provide for increased opportunities for visitation to those residing in long-term residential care facilities (LTRCs). The HSE has also advised that healthcare workers that they do not have to restrict movements if they are a close contact of a confirmed COVID-19 case (with the exceptions of VoCs). Furthermore, the HSE has updated its guidance for those previously advised to cocoon, about activities they may wish to consider resuming once fully vaccinated. More recently, the requirement for mandatory hotel quarantine for those returning from category 2 countries has been lifted for fully vaccinated individuals, however the requirement for a period of home quarantine remains in place.

The (EMA) safety committee (PRAC) has recently concluded that unusual blood clots with low blood platelets (thrombosis with thrombocytopenia syndrome, or TTS) should be listed as very rare side effects of both the COVID-19 Vaccine Vaxzevria® and COVID-19 Vaccine Janssen®. The National Immunisation Advisory Committee (NIAC) considers the benefit/risk ratio of both these vaccines is favourable in all ages and is very clearly demonstrated in those aged 50 years and older, even when virus circulation is reducing in the community. As the risks of TTS may be higher in younger adults, and as alternative COVID-19 vaccines are available, NIAC has advised that these vaccines should be offered to those aged 50 years and older, with the exception of immunocompromised individuals who are recommended to receive an MRNA vaccine. NIAC have also advised that those aged 50 years and older who have already received their first dose of Vaxzevria®, as well as those under 50 years at very high or high risk of severe COVID-19 disease, should receive their second dose at 12 weeks as scheduled. Those under 50 years of age without a very high or high risk of severe COVID-19 disease

3 Guidance on vaccinated individuals visiting other vaccinated individuals in a household setting (v.1 31/3/21)
4 COVID-19 Guidance on visits to Long Term Residential Care Facilities (LTRCFs). (v.2 23/04/21)
should have their second dose 16 weeks after the first dose to allow for assessment of emerging evidence regarding the risk and benefits of the second dose of this vaccine.

**Evidence one dose Vaxzevria® COVID-19 vaccine**

In their advices of April 26th to the CMO, it was also noted by NIAC that three weeks after one dose of Vaxzevria®, levels of protection are comparable to that after one dose of COVID-19 vaccine Janssen® and this protection persists for at least 12 weeks.

Pooled analysis of four randomised clinical trials have demonstrated that vaccine efficacy against symptomatic COVI-19 after a single standard dose of Vaxzevria® was 76·0% (59·3–85·9) from day 22 to day 90 after vaccination. Modelling analysis indicated that protection did not wane during the initial 3-month period. Similarly, antibody levels were maintained during this period with minimal waning by day 90.

This compares to an efficacy of 76% against severe-critical COVID-19, 14-days post vaccination with COVID-19 Vaccine Janssen® in randomised, double-blind, placebo-controlled phase III trial. A slightly lower efficacy of 66.9% and 66.1% was observed for moderate-severe-critical COVID-19, 14- and 28-days post-vaccination, respectively. No meaningful differences in vaccine efficacy were observed among subgroups defined according to sex, race, or ethnic group. A lower point estimate of vaccine efficacy was observed among participants 60 years of age or older with coexisting co conditions in the analysis of cases with onset at least 28 days after administration.

There have been a number of observational trials, which have also provided data regarding the efficacy of, and immunological response to one dose of Vaxzevria® vaccine. The odds (CI 95%) of a new PCR-positive test were reduced by 64% in those ≥21 days after vaccination with a single dose of Vaxzevria® compared to those not vaccinated or previously PCR/antibody positive. Public Health England have reported vaccine effectiveness of 58% 35 days after administration of a single dose of Vaxzevria® in those over 70 years. Similarly, Bernal et al have reported vaccine effects in older adults (≥70 years) were seen from 14-20 days after vaccination reaching an effectiveness of 60% from 28-34 days and further increasing to 73% from day 35 onwards. A single dose of Vaxzevria® has also been found to be 94% effective in reducing COVID-19 related hospitalisations 28-34 days post-vaccination.

It should be noted that all clinical trials and post marketing are based on a two-dose schedule of Vaxzevria® with efficacy of the vaccine increasing with a longer dose interval between the first and second doses.

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7 Lancet 2021 one phase 1/2 study in the UK (COV001), one phase 2/3 study in the UK (COV002), and a phase 3 study in Brazil (COV003)—and one double-blind phase 1/2 study in South Africa (COV005).
8 Sandoff J et al NEJM April 21 2021
9 Pritchard E et al. Vaccine Effectiveness Study UK Impact of vaccination on SARS-CoV-2 cases in the community: a population-based study using the UK’s COVID-19 Infection Survey (Pre-print 23-04-21)
10 Public Health England vaccine effectiveness report (March 2021)
11 Bernal et al. Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in England. Lancet (Pre-print 02-03-21).
12 Vasileiou Eas et al. Effectiveness of First Dose of COVID-19 Vaccines Against Hospital Admissions in Scotland: National Prospective Cohort Study of 5.4 Million People. The Lancet (Pre-print 30-12-20)
second dose (efficacy of 55.1% versus 81.3% against symptomatic COVID-19 disease at <6 weeks and ≥12 weeks respectively). In the view of NIAC, there is insufficient evidence to support consideration to a change from the authorised two-dose Vaxzevria® schedule. The second dose of Vaxzevria® is considered essential to enhance durability of protection.

Proposal

Following NIAC advice, those aged 50 years and older (including those at very- and high-risk of serious disease) can receive any of the four currently authorised EMA vaccines. A person is considered fully vaccinated 7 days after the second dose of COVID-19 Pfizer (Comirnaty®) vaccine; 14 days after the single dose of Janssen® and the second Moderna dose; 15 days after the second dose of Vaxzevria®. The dose interval for the two mRNA vaccines is currently 28 days and for Vaxzevria® is the interval is currently 12 weeks (and 16 weeks for those under 50 years of age without a very high or high risk of severe COVID-19 disease, who have already received a first dose). In light of recent measures to provide a vaccine dividend to those individuals who are fully vaccinated, the significantly longer dosing interval for Vaxzevria® as compared to the mRNA vaccines and Janssen®, could act as a disincentive for people to accept vaccination with Vaxzevria®. This could have an overall negative effect on the roll out of the vaccine programme.

Thus, it is being proposed that public health guidance relating to those who are fully vaccinated, with the exception of that relating to foreign travel, will be applicable to those 4 weeks (28 days) after having received a first dose of COVID-19 Vaccine Vaxzevria®. Notwithstanding, the applicability of this guidance, it is essential that individuals continue to receive their full course of vaccination.