Annex A: Report to JCVI on estimated efficacy of a single dose of Pfizer BioNTech (BNT162b2 mRNA) vaccine and of a single dose of ChAdOx1 vaccine (AZD1222)

Public Health England

1. Introduction

This report outlines the estimated single dose vaccine efficacy (VE) of the Pfizer and ChAdOx1 Covid-19 vaccines as discussed at the JCVI COVID-19 sub-group meeting of December 22nd December 2020. The ChAdOx1 estimates were presented by the Oxford team to the JCVI COVDI-19 sub-committee in a presentation and also in a clinical overview document. The Pfizer estimates were verbally given by PHE during discussion and were based on data previously provided to the sub-committee.

2. Pfizer single dose VE

In the published phase III efficacy paper [1] the VE primary end point for Covid-19 at least 7 days after a second dose was 95.0% (95% Confidence Interval: 90.3-97.6) and when including those with evidence of prior infection at baseline 94.6% (89.9-97.3).

In Figure 3 single dose VE at any time after dose 1 and before dose 2 was given as 52.4% (29.5-68.4) [39 events in the vaccine arm and 82 placebo]. For the period 2 to 7 days after dose 2 it was given as 90.5% (61.0-98.8) [2 events vs 21].

The 52.4% figure, however, includes COID-19 infections occurring shortly after the first dose, an interval within which this dose would not be expected to have had an effect (i.e prior to the recipient mounting an immune response). Figure 3 clearly shows that from approximately 10 days after the first dose the cumulative incidence in the vaccine and Placebo groups diverge. It would therefore be appropriate to calculate the VE of a single dose in a period after this 10 days.

A reasonable interval to use for post first dose VE would therefore be from >14 days to the time of the second dose (scheduled 21 days after the first dose) or to 7 days after the second dose base on the assumption the second dose would not have induced a response in this interval. Unfortunately, this analysis is not presented in the paper. The fact that the slope of the placebo and vaccine arms appears similar in figure 3 as person time moves from 10 days post 1 to post 2 doses suggests that VE is fairly similar from at least 10 days post dose 1 and post dose2.

The numbers at each 7-day cumulative interval behind figure 3 of the published paper are given in Figure 1 below which is taken from the *Emergency Use Authorization for Pfizer-BioNTech COVID-19 Vaccine Review Memo (fda.gov)*. These were as follows at days 14, 21- and 28-days post dose 1:

	Cumulative cases	
Days after dose 1	**Vaccine n/N**	**Placebo n/N**
14	37/21054	55/20970
21	39/20481	73/20366
28	41/19314	97/19209

VE of a single dose for the intervals 15-21, 22-28 and 15-28 days after the first dose is therefore as given in table 1 below (using the denominator at the day 21 time point).

Table1: VE in intervals post the first dose where protection from only this dose may be expected.

	Pfizer vaccine		Placebo		VE (95% CI)
Post dose 1 interval	N	N	N	N	
15-21 days	2	20481	18	20366	89% (52-97)
22-28 days	2	20481	24	20366	92% (65-98)
15-28 days	4	20481	42	20366	91% (74-97)

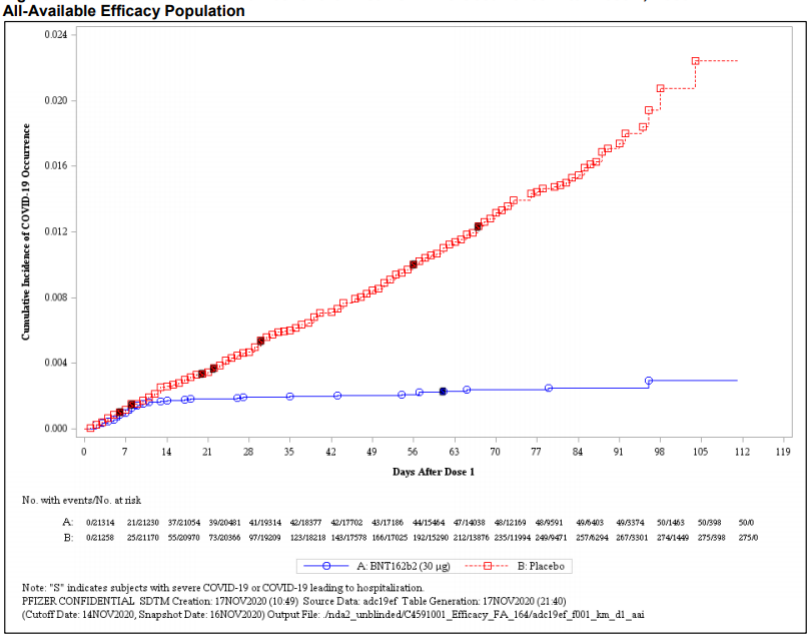
Note that the 15-21 day interval is prior to the scheduled second dose. The 22-28 day interval is in a period where the second dose will have been given to many participants but is prior to the time protection may be expected from the second dose. The numbers for this 22-28 day interval are similar to the reported numbers of 2 v 21 given in Figure 3 of the publication for the interval 2 to 7 days after dose2.

This analysis therefore indicates a VE of about 90% from 2 weeks after the first dose and for the following 2 weeks. It does not indicate VE beyond this time point as participants had received a second dose. Assuming the period up to 7 days post the second dose is still dose 1 protection then the VE is at least 74% (bottom end of 95%CI). This estimate of ~ 90% is much higher than the 52.4% reported in the paper where the early cases post the first dose were included.

Figure 1 – Cumulative incidence curves for the first COVID-19 occurrence after dose 1

Taken from Emergency Use Authorization for Pfizer-BioNTech COVID-19 Vaccine Review Memo (fda.gov)

Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1, Dose 1
All-Available Efficacy Population



3. ChadOx1 single dose VE

MHRA Information for Healthcare Professionals on COVID-19 Vaccine AstraZeneca states:

The level of protection gained from a single dose of COVID-19 Vaccine AstraZeneca was assessed in an exploratory analysis that included participants who had received one dose. Participants were censored from the analysis at the earliest time point of when they received a second dose or at 12 weeks post dose 1. In this population, vaccine efficacy from 22 days post dose 1 was 73.00% (95% CI: 48.79; 85.76 [COVID-19 Vaccine AstraZeneca 12/7,998 vs control 44/7,982]).

Exploratory analyses showed that increased immunogenicity was associated with a longer dose interval (see Immunogenicity Table 3). Efficacy is currently demonstrated with more certainty for dose intervals from 8 to 12 weeks. Data for intervals longer than 12 weeks are limited.

4. Moderna

The details below are taken from Vaccines and Related Biological Products Advisory Committee December 17, 2020 Meeting Briefing Document - FDA. This shows that from 15 days after the first dose to the time of the second dose VE was 92.1% (68.8%-99.1%). Cumulative cases show a divergence between the vaccine and placebo groups from about 14 days after the first dose (Figure 2)

Additional Interim Efficacy Analyses

Additional analyses were done to assess efficacy against COVID-19 after one dose of mRNA1273. In participants in the mITT set who only received one dose of the vaccine at the time of the interim analysis, VE after one dose was 80.2% (95% CI 55.2%, 92.5%). These participants had a median follow-up time of 28 days (range: 1 to 108 days). The small, non-random sample and short median follow-up time limits the interpretation of these results. There appears to be some protection against COVID-19 disease following one dose; however, these data do not provide sufficient information about longer term protection beyond 28 days after a single dose.

Table 15. Vaccine Efficacya of mRNA-1273 to Prevent COVID-19 From Dose 1 by Time Period in Participants Who Only Received One Dose, mITT Set

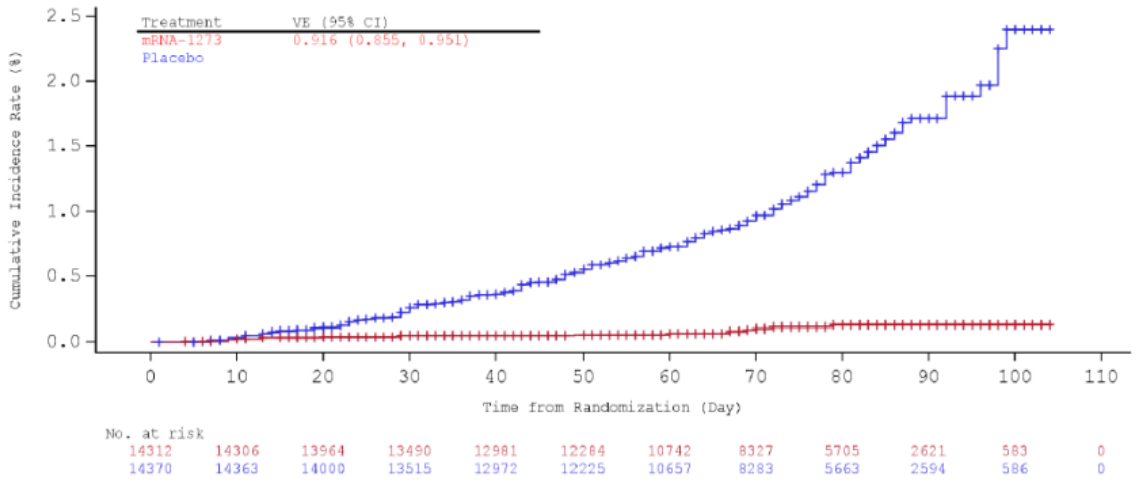
First COVID-19 Occurrence After Dose 1	Vaccine Group N=996 Case n (%)	Placebo Group N=1079 Case n (%)	VE (%) (95% CI)*
After dose 1	7/996 (87.5)	39/1079 (96.7)	80.2% (55.2%, 92.5%)
After dose 1 to 14 days after dose 1	5/996 (38.0)	11/1079 (41.1)	50.8% (-53.6%, 86.6%)
>14 days after dose 1**	2/983 (87.2)	28/1059 (96.2)	92.1% (68.8%, 99.1%)

Surveillance time in person years for given endpoint across all participants within each group at risk for the endpoint
* VE is calculated as 1-ratio of incidence rates (mRNA-1273/Placebo). The 95% CI of VE is calculated using the exact method conditional upon the total number of cases, adjusting for person-years
**Participants who were not at risk (cases or censored at prior time period) are excluded from this analysis
[a] Based on interim analysis: Novemer 7, 2020 efficacy data cutoff.

Figure 2 – Cumulative incidence curves for the first COVID-19 occurrence after randomisation

Taken from Vaccines and Related Biological Products Advisory Committee December 17, 2020 Meeting Briefing Document - FDA

Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Randomization, mITT Set



[1] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020 Dec 10:NEJMoa2034577. doi: 10.1056/NEJMoa2034577.

[2] Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, Angus B, 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. Lancet. 2020 Dec 8:S0140-6736(20)32661-1. doi: 10.1016/S0140-6736(20)32661-1.

[3] Emergency Use Authorization for Pfizer-BioNTech COVID-19 Vaccine Review Memo (fda.gov)

[4] Vaccines and Related Biological Products Advisory Committee December 17, 2020 Meeting Briefing Document - FDA

[5] https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca/information-for-healthcare-professionals-on-covid-19-vaccine-astrazeneca