4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Comirnaty is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 virus, in individuals 16 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

4.2 Posology and method of administration

Posology

Individuals 16 years of age and older
Comirnaty is administered intramuscularly after dilution as a course of 2 doses (0.3 mL each). It is recommended to administer the second dose 3 weeks after the first dose (see sections 4.4 and 5.1).

There are no data available on the interchangeability of Comirnaty with other COVID-19 vaccines to complete the vaccination course. Individuals who have received 1 dose of Comirnaty should receive a second dose of Comirnaty to complete the vaccination course.

Paediatric population
The safety and efficacy of Comirnaty in children and adolescents aged less than 16 years of age have not yet been established. Limited data are available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccines, other viral vaccines, ATC code: J07BX03

Mechanism of action

The nucleoside-modified messenger RNA in Comirnaty is formulated in lipid nanoparticles, which enable delivery of the non replicating RNA into host cells to direct transient expression of the SARS-CoV-2 S antigen. The mRNA codes for membrane-anchored, full-length S with two point mutations within the central helix. Mutation of these two amino acids to proline locks S in an antigenically preferred prefusion conformation. The vaccine elicits both neutralizing antibody and cellular immune responses to the spike (S) antigen, which may contribute to protection against COVID-19.

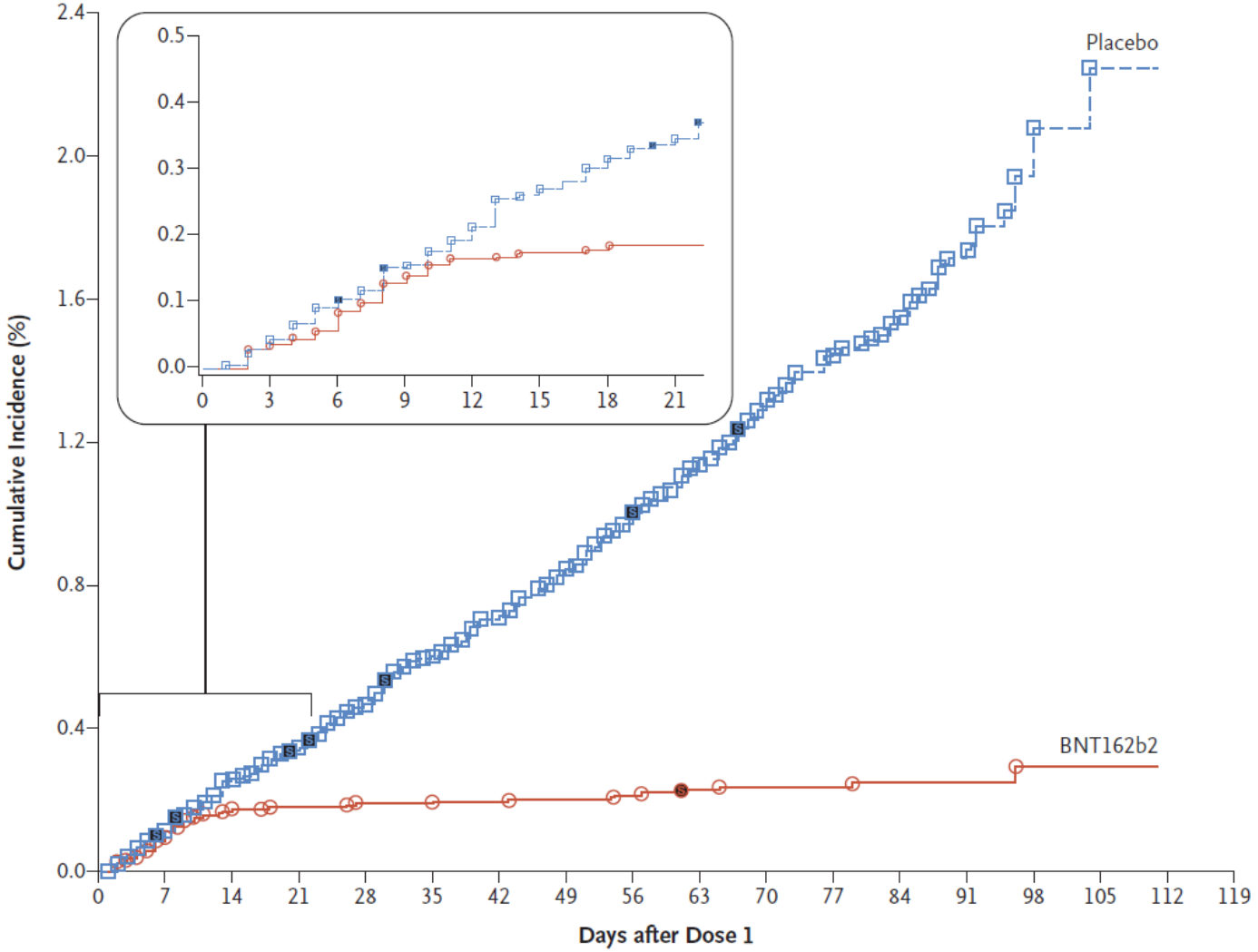
Efficacy

Study 2 is a multicentre, multinational, Phase 1/2/3 randomised, placebo-controlled, observer-blind dose-finding, vaccine candidate selection and efficacy study in participants 12 years of age and older. Randomisation was stratified by age: 12 through 15 years of age, 16 through 55 years of age, or 56 years of age and older, with a minimum of 40% of participants in the ≥ 56-year stratum. The study excluded participants who were immunocompromised and those who had previous clinical or microbiological diagnosis of COVID-19. Participants with pre-existing stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrolment, were included as were participants with known stable infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV) or hepatitis B virus (HBV). At the time of the analysis of Study 2, information presented is based on participants 16 years and older.

Efficacy in participants 16 years of age and older

In the Phase 2/3 portion, approximately 44,000 participants were randomised equally and were to receive 2 doses of COVID-19 mRNA Vaccine or placebo separated by 21 days. The efficacy analyses included participants that received their second vaccination within 19 to 42 days after their first vaccination. The majority (93.1%) of vaccine recipients received the second dose 19 days to 23 days after Dose 1. Participants are planned to be followed for up to 24 months after Dose 2, for assessments of safety and efficacy against COVID-19. In the clinical study, participants were required to observe a

EMA approval – Annex I - SUMMARY OF PRODUCT CHARACTERISTICS



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time *person-yr (no. at risk)*	No. of participants	Surveillance time *person-yr (no. at risk)*	*percent*
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.

Shown is the cumulative incidence of Covid-19 after the first dose (modified intention-to-treat population). Each symbol represents Covid-19 cases starting on a given day; filled symbols represent severe Covid-19 cases. Some symbols represent more than one case, owing to overlapping dates. The inset shows the same data on an enlarged y axis, through 21 days. Surveillance time is the total time in 1000 person-years for the given end point across all participants within each group at risk for the end point. The time period for Covid-19 case accrual is from the first dose to the end of the surveillance period. The confidence interval (CI) for vaccine efficacy (VE) is derived according to the Clopper–Pearson method.

Polack et al., NEJM 2020

Public health impact of delaying second dose of BNT162b2 or mRNA-1273 covid-19 vaccine: simulation agent based modeling study

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ABSTRACT

OBJECTIVE

To estimate population health outcomes with delayed second dose versus standard schedule of SARS-CoV-2 mRNA vaccination.

DESIGN

Simulation agent based modeling study.

SETTING

Simulated population based on real world US county.

PARTICIPANTS

The simulation included 100 000 agents, with a representative distribution of demographics and occupations. Networks of contacts were established to simulate potentially infectious interactions though occupation, household, and random interactions.

INTERVENTIONS

Simulation of standard covid-19 vaccination versus delayed second dose vaccination prioritizing the first dose. The simulation runs were replicated 10 times. Sensitivity analyses included first dose vaccine efficacy of 50%, 60%, 70%, 80%, and 90% after day 12 post-vaccination; vaccination rate of 0.1%, 0.3%, and 1% of population per day; assuming the vaccine prevents only symptoms but not asymptomatic spread (that is, non-sterilizing vaccine); and an alternative vaccination strategy that implements delayed second dose for people under 65 years of age, but not until all those above this age have been vaccinated.

MAIN OUTCOME MEASURES

Cumulative covid-19 mortality, cumulative SARS-CoV-2 infections, and cumulative hospital admissions due to covid-19 over 180 days.

RESULTS

Over all simulation replications, the median cumulative mortality per 100 000 for standard dosing versus delayed second dose was 226 *v* 179, 233 *v* 207, and 235 *v* 236 for 90%, 80%, and 70% first dose efficacy, respectively. The delayed second dose strategy was optimal for vaccine efficacies at or above 80% and vaccination rates at or below 0.3% of the population per day, under both sterilizing and non-sterilizing vaccine assumptions, resulting in absolute cumulative mortality reductions between 26 and 47 per 100 000. The delayed second dose strategy for people under 65 performed consistently well under all vaccination rates tested.

CONCLUSIONS

A delayed second dose vaccination strategy, at least for people aged under 65, could result in reduced cumulative mortality under certain conditions.

Evaluation of COVID-19 vaccination strategies with a delayed second dose

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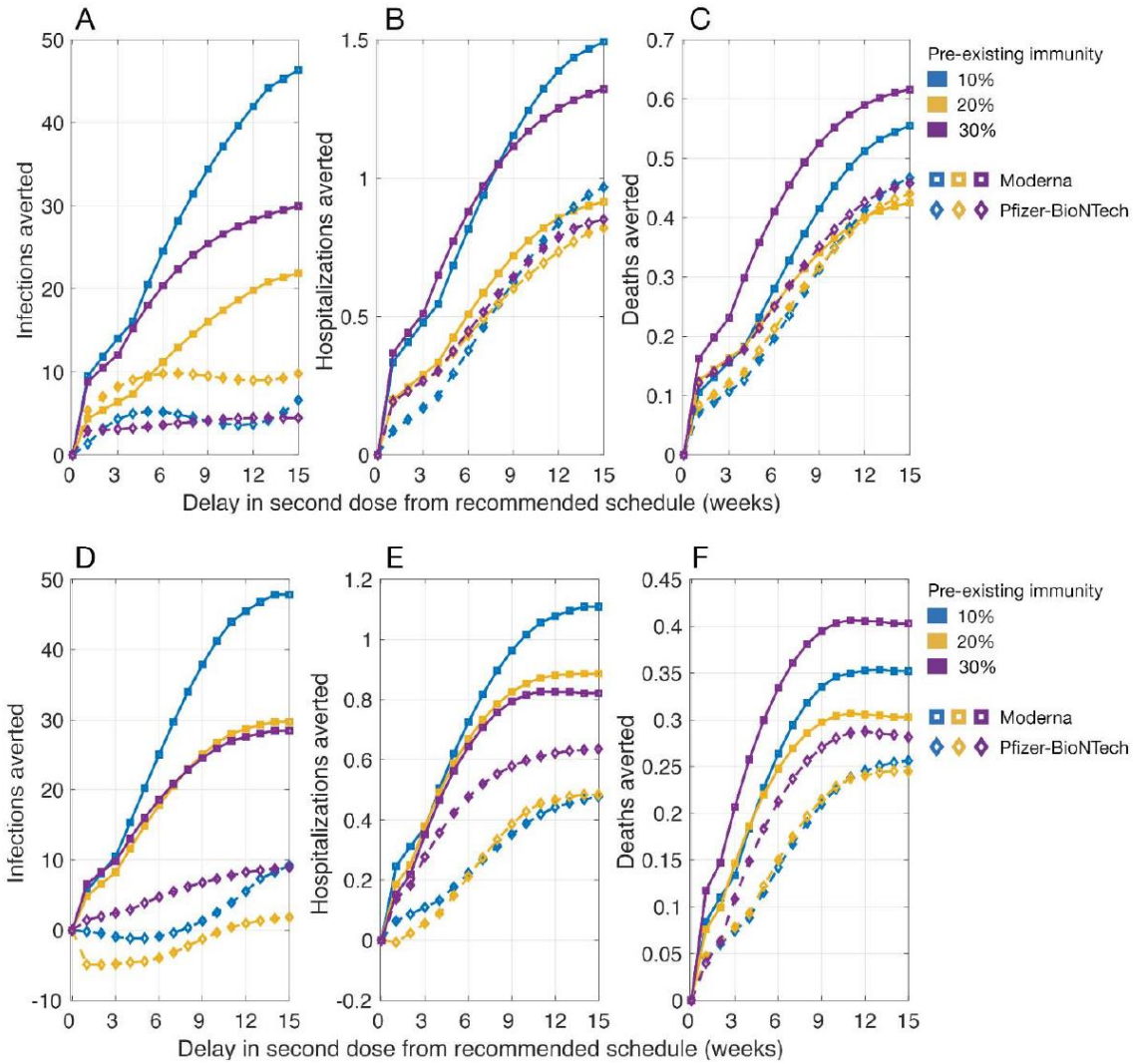

Figure 2. Projected number of infections, hospitalizations, and deaths averted per 10,000 population in a DSD vaccination program compared to the recommended schedule of two-doses of Moderna (with a 28-day interval) and Pfizer-BioNTech (with a 21-day interval) vaccines. The daily vaccination rate was (A,B,C) 30 doses and (D,E,F) 45 doses per 10,000 population. Vaccine efficacy was set to the mean of estimated ranges (Figure 1) without waning of the first dose efficacy prior to the administration of the second dose.

NEWS · 13 MAY 2021

Delaying a COVID vaccine's second dose boosts immune response

Older people who waited 11–12 weeks for their second jab had higher peak antibody levels than did those who waited only 3 weeks.

Heidi Ledford

But for some existing vaccines, a longer wait between first and second doses yields a stronger immune response. Delaying the COVID-19 booster shots could also expand partial immunity among a greater swathe of the population than could the shorter dosing schedule. On 30 December, the United Kingdom announced that it would delay the second dose by up to 12 weeks after the first.

To determine whether the delay paid off, Amirthalingam and her colleagues studied 175 vaccine recipients older than 80 who received their second dose of the Pfizer vaccine either 3 weeks or 11–12 weeks after the first dose. The team measured recipients' levels of antibodies against the SARS-CoV-2 spike protein and assessed how immune cells called T cells, which can help to maintain antibody levels over time, responded to vaccination.

Peak antibody levels were 3.5 times higher in those who waited 12 weeks for their booster shot than were those in people who waited only 3 weeks. Peak T-cell response was lower in those with the extended interval. But this did not cause antibody levels to decline more quickly over the nine weeks after the booster shot.

The results are reassuring, but are specific to the Pfizer vaccine, which is not available in many low-to-middle income countries, says Alejandro Cravioto, chair of the World Health Organization's Strategic Advisory Group of Experts on Immunization. Countries will need to consider whether the variants that are circulating in their particular region might raise infection risk after only one vaccine dose, he says.

Why Oxford's positive COVID vaccine results are puzzling scientists

Subjects

Public health | Vaccines | Immunology | SARS-CoV-2

Extended interval BNT162b2 vaccination enhances peak antibody generation in older people

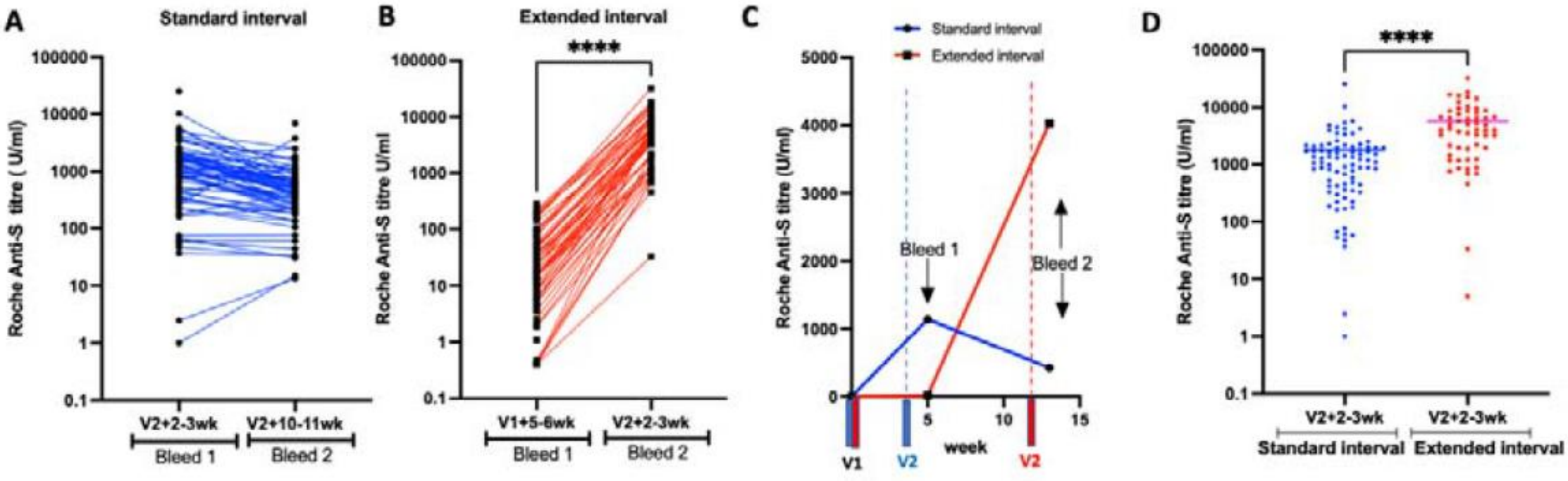

Figure 2. Extended-interval vaccination with BNT162b2 stimulates stronger peak spike-specific antibody responses

Parry H at al.
medRxiv preprint doi: https://doi.org/10.1101/2021.05.15.21257017;