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Vaccine Development in Global Pandemic Time

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1. Introduction

Pfizer-BioNTech collaboration started in 2018 in order to develop mRNA flu vaccine. Because of the covid19 pandemic the two companies started to focus on mRNA vaccine development for the prevention of covid19 infection. In March they signed the Letters of Intent. Initially there were four vaccine candidates including unmodified mRNA, nucleoside-modified mRNA and self-amplifying mRNA. For further development the nucleoside-modified mRNA was chosen. In April Phase 1/2 study was completed in Germany and in May in the USA. Two 30 μg doses 3 weeks apart induced neutralizing antibody titers comparable to natural infection and strong CD4+ and CD8+ T-cell responses were observed. Phase 2b/3 clinical trial started in July involving more than 43.000 participants in 153 sites. The result showed 95% efficacy with mild and moderate local and systemic events. For safety reason all participants will be followed for 2 years after the second dose. Based on rolling review regulatory agencies were able to approve within a short period of time in December 2020, first MHRA in UK, then FDA authorized for Emergency Use and EMA granted Conditional Marketing Authorization on 21 December 2021 for 16 years old and older.

The first shipments were sent all European countries on 27 December. Direct shipments to vaccination centers on ultra-low temperature (minus 90—60 degree of centigrade) using dry ice. Each thermal shipping container has a temperature monitoring device. All shipments are tracked via GPS monitoring device to ensure end-to-end distribution within required temperatures.

In May EMA granted an extension of indication for covid-19 vaccine to include in children aged 12-15. The effect of vaccine was investigated in 2260 children aged 12-15, about half of them received dummy injection. Of the 1,005 children receiving the vaccine, none developed COVID-19 compared to 16 children out of the 978 who received the dummy injection. This means that, in this study, the vaccine was 100% effective at preventing COVID-19.

The most common side effects in children aged 12 to 15 are similar like those in people aged 16 and above. They include pain at the injection site, tiredness, headache, muscle and joint pain, chills and fever. These effects are usually mild or moderate and improve within a few days from the vaccination.

Initial vaccine candidates

Variant	Target	RNA Construct	Regimen
162a1	RBD subunit	uRNA	Prime/boost
162b1	RBD subunit	modRNA	Prime/boost
162b2	P2-mutated* full spike protein	modRNA	Prime/boost
162c2	P2-mutated* full spike protein	saRNA	Single injection

EMA granted approval for booster dose (third dose) for immune weakened people 28 days after the second dose, and 6 months after the second dose for 18 years of age and older.

Approval is based on the clinical program evaluating the safety, tolerability and immunogenicity of a booster dose of covid-19 vaccine. A booster dose of the vaccine elicited significantly higher neutralizing antibody titers against the initial SARS-CoV-2 virus (wild type), as well as the Beta and Delta variants, when compared with the levels observed after the two-dose primary series. The reactogenicity profile within seven days after the booster dose was typically mild to moderate, and the frequency of reactions was similar to or lower than after dose two. The efficacy is this trial was 95,6%.

In October 2021 FDA authorized for emergency use of covid-19 for children 5 through 111 years of age. For this age group, the vaccine is to be admin-

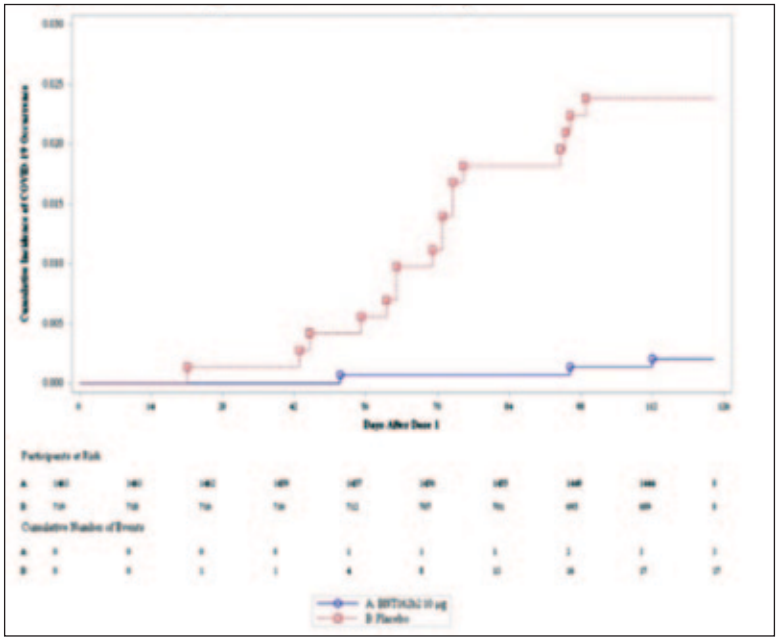

Figure 1 *Commulative Incidence Curves for the First COVID-19 Occurance After Dose 1–Phase 2/3 Initial Enrollment Group – 5 to <12 Years of Age – Dose 1 AB-Available Efficiacy Population*

istered in a two-dose regimen of 10 μg (0,2 ml) doses given 21 days apart. EUA is supported by clinical data showing a favorable safety profile and high vaccine efficacy of 90.7% in children 5 through 11 years of age during a period when Delta was the prevalent strain.

In 2021 we have already distributed 1,8B doses to 146 countries by end of September. In 2022 we plan to distribute 4B doses.

References

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