BNT162b2 Vaccine Candidate Against COVID-19

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Pfizer-BioNTech COVID-19 Vaccine Development Overview:

KEY CLINICAL DEVELOPMENTAL MILESTONES:

REGULATORY AUTHORIZATIONS (selected, additional countries pending regulatory review):

March 17
PFE/BNT Letters of Intent

April 23
Phase 1/2 Trial Germany

May 4
Phase 1/2 Trial US

July 27
Pivotal Phase 2b/3 Trial

November 18
Phase 3 Study Meets Primary Efficacy Endpoints

December 02
UK Reg 174 by MHRA

December 11
US EUA by FDA

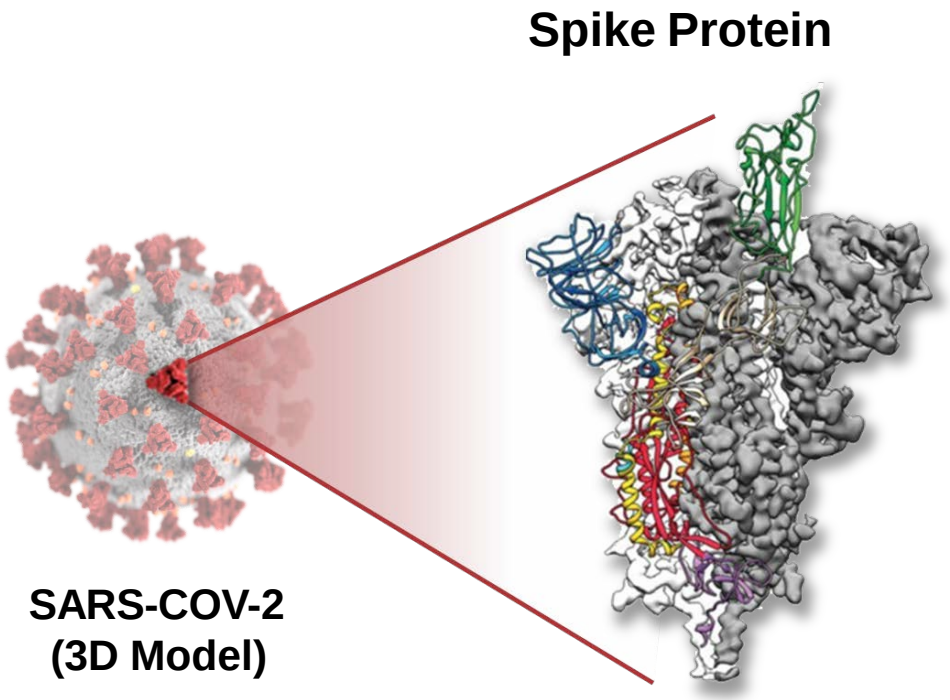
December 19
Switzerland TMA by Swissmedic

December 21
EMA CMA by EC

December 31
WHO Emergency Use Listing

https://www.pfizer.com/news. Accessed December 22, 2020

Selection of Pfizer/BioNTech COVID-19 Vaccine BNT162b2



Initially Four Vaccine Candidates

	Variant	Target	RNA Construct	Regimen
1	162a1	RBD subunit	uRNA	Prime/boost
2	162b1	RBD subunit	modRNA	Prime/boost
3	**162b2**	**P2-mutated full spike protein**	**modRNA**	**Prime/boost**
4	162c2	P2-mutated full spike protein	saRNA	Single injection

uRNA: unmodified mRNA
modRNA: nucleoside modified mRNA saRNA: self-amplifying mRNA
1. Wrapp et al., 2020, *Science.*

Phase 2/3 Global Study

Safety, Tolerability, Immunogenicity, and Efficacy of RNA Vaccine Candidates Against COVID-19 in Healthy Adults – Phase 2/3 study start July 27, 2020[1,2]

Design

- Randomized, placebo-controlled (1:1), blinded (participant, care provider, investigator)
- Candidate: RNA (modRNA) BNT162b2
- 30µg dose, IM
- 2 dose regimen separated by 21 days
- Approximately 44,000 participants
- Age: ≥12 years of age (Phase 2/3)
  - Stratified as 12-15, 16-55, or >55 years of age
- 152 clinical trial sites globally in the U.S, Argentina, Brazil, South Africa, Turkey and Germany.[3]

Objectives

- Safety, immunogenicity, and efficacy
- Primary endpoints include:
  - Prevention of COVID-19 in those who have not been infected by SARS-CoV-2 prior to immunization
  - Prevention of COVID-19 regardless of whether participants have previously been infected by SARS-CoV-2
- Primary efficacy analysis is event-driven based on the number of participants with symptomatic COVID-19 disease

Trial Expansion[1,4]

- Pfizer and BioNTech expanded the pivotal COVID-19 vaccine trial to increase trial population diversity and include adolescents as young as 12 years of age and people with chronic, stable HIV, Hepatitis C, or Hepatitis B infection, as well as provide additional safety & efficacy data.

1. ClinicalTrials.gov. Available from https://clinicaltrials.gov/ct2/show/NCT04368728?term=NCT04368728&draw=2&rank=1 Accessed Dec 13, 2020. 2. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-choose-lead-mrna-vaccine-candidate-0.. 3. Polack FP, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine N Engl J Med. 2020 Dec 10 4. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-propose-expansion-pivotal-covid-19 Accessed October 13, 2020

Adverse reactions from clinical studies (as presented in EMA SmPC):

System Organ Class	Very common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1,000 to < 1/100)	Rare (≥ 1/10,000 to < 1/1,000)	Not known (cannot be estimated from the available data)
Blood and lymphatic system disorders			Lymphadenopathy		
Immune system disorders					Anaphylaxis; hypersensitivity
Psychiatric disorders			Insomnia		
Nervous system disorders	Headache			Acute peripheral facial paralysis†	
Gastrointestinal disorders		Nausea			
Musculoskeletal and connective tissue disorders	Arthralgia; myalgia		Pain in extremity		
General disorders and administration site conditions	Injection site pain; fatigue; chills; pyrexia*; injection site swelling	Injection site redness	Malaise; injection site pruritus		

*A higher frequency of pyrexia was observed after the 2nd dose.
† Throughout the safety follow-up period to date, acute peripheral facial paralysis (or palsy) was reported by four participants in the COVID-19 mRNA Vaccine group. Onset was Day 37 after Dose 1 (participant did not receive Dose 2) and Days 3, 9, and 48 after Dose 2. No cases of acute peripheral facial paralysis (or palsy) were reported in the placebo group. The safety profile in 545 subjects receiving Comirnaty, that were seropositive for SARS-CoV-2 at baseline, was similar to that seen in the general population.

Reference: EMA Summary of Product Characteristics Dec 2020, available at https://www.ema.europa.eu/en (accessed 22 Dec 2020)

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

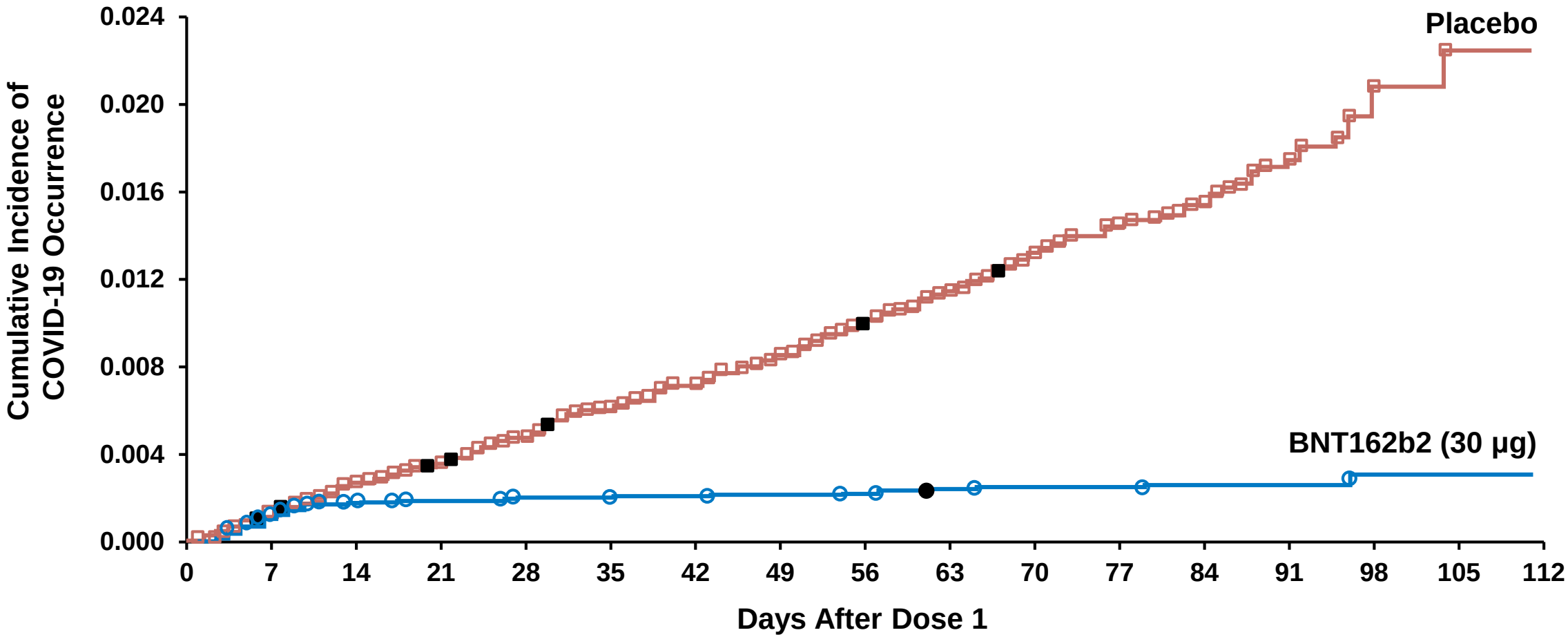
	Pfizer-BioNTech COVID-19 Vaccine (30 µg) N=18,198		Placebo N=18,325				
Efficacy Endpoint	**n**	**Surveillance Time (n)**	**n**	**Surveillance Time (n)**	**VE (%)**	**(95% CI)**	**Pr (VE >30%)**
First COVID-19 occurrence >7 days after Dose 2	**8**	**2.214 (17,411)**	**162**	**2.222 (17,511)**	**95.0**	**(90.3, 97.6)**	**>0.9999**

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint..
Pr=Posterior probability

Pfizer Medical

Polack FP, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine N Engl J Med. 2020 Dec 10.

Cumulative Incidence of COVID-19 After Dose 1



Filled symbols indicates subjects with severe COVID-19 per FDA definition

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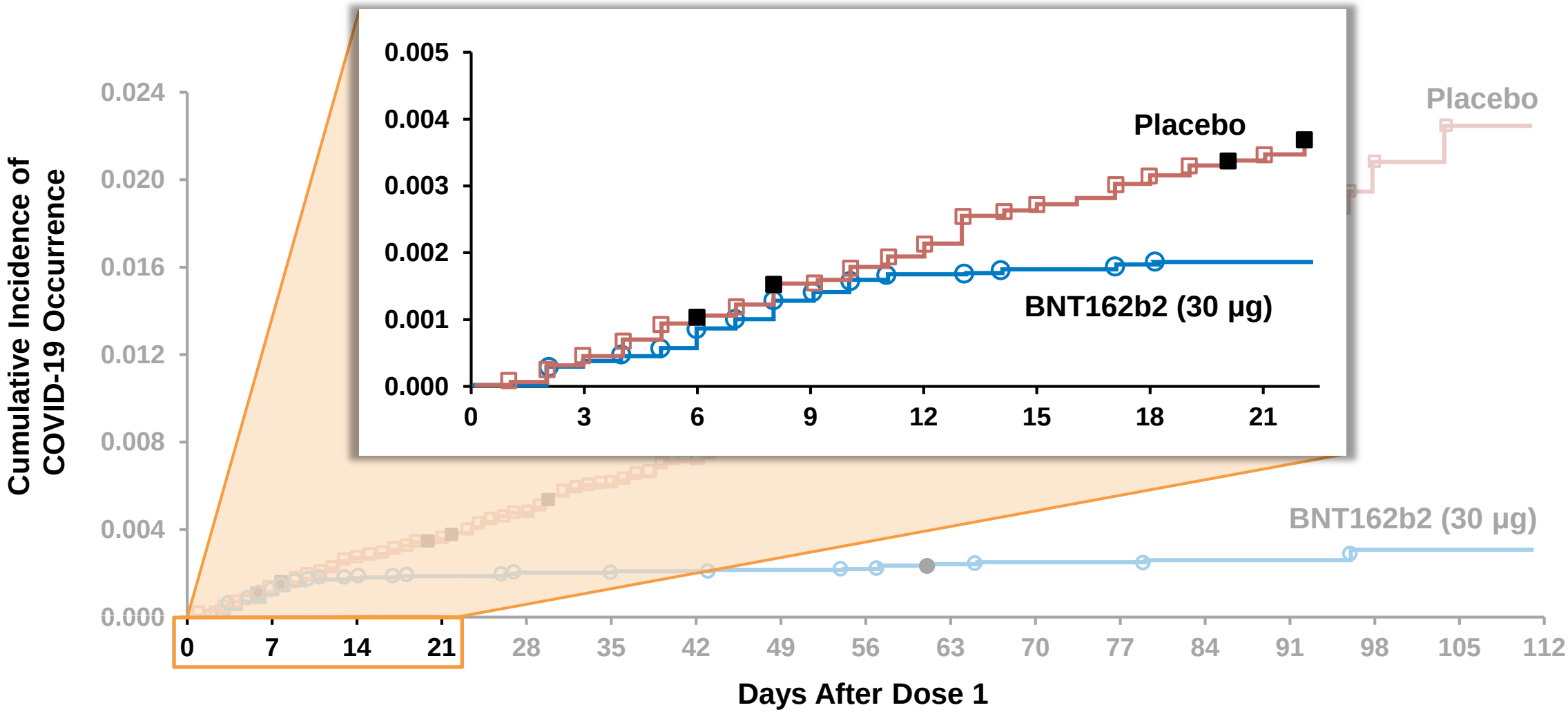
Cumulative Incidence of COVID-19 After Dose 1



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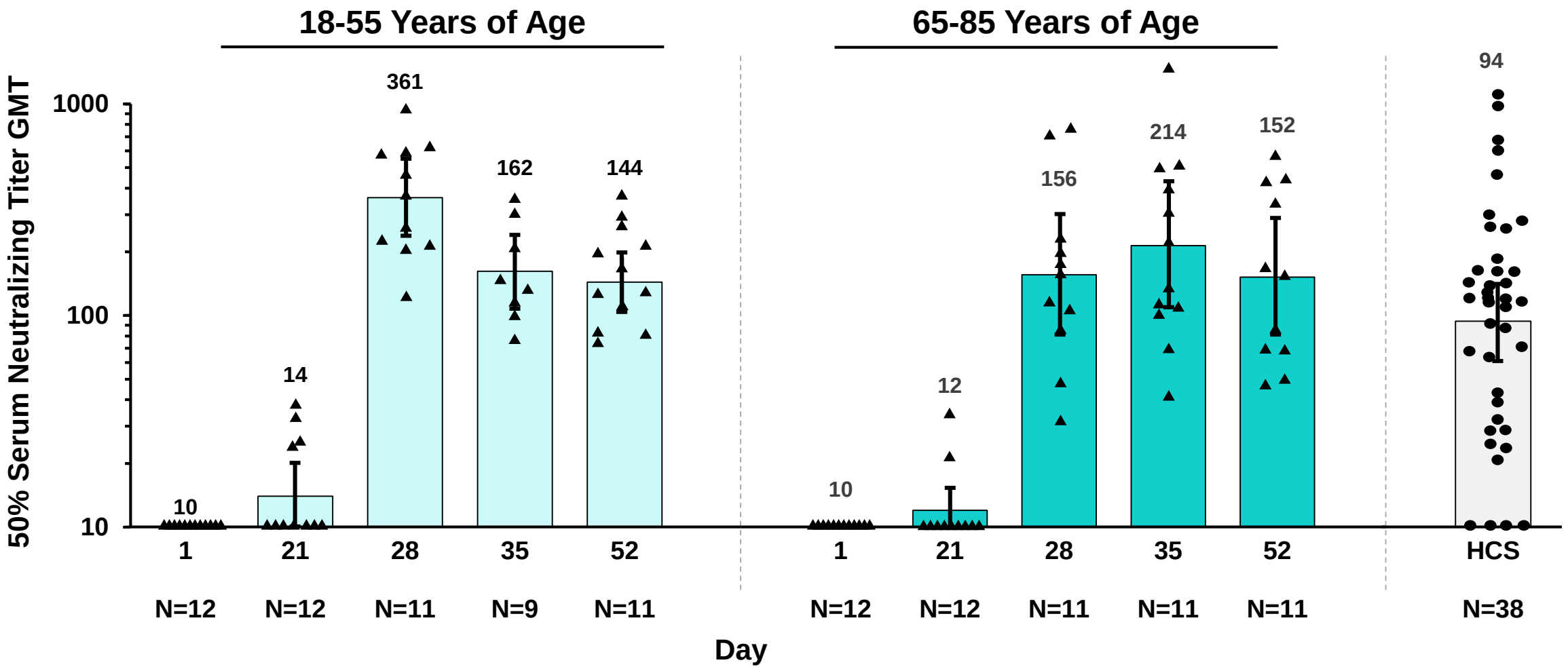
Two 30 µg Doses of BNT162b2 Induce Neutralizing Antibody Titers Comparable or Higher than Natural Infection



Graphic adapted from Walsh EE, et al. *N Engl J Med*. 2020

First COVID-19 Occurrence After Dose 1

	Pfizer-BioNTech COVID-19 Vaccine (30 µg) N=21,669 n	Placebo N=21,686 n	VE (%)	(95% CI)
COVID-19 occurrence after Dose 1	50	275	82.0	(75.6, 86.9)
After Dose 1 and 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)

Pfizer Medical

Polack FP, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine N Engl J Med. 2020 Dec 10.