2019 Update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

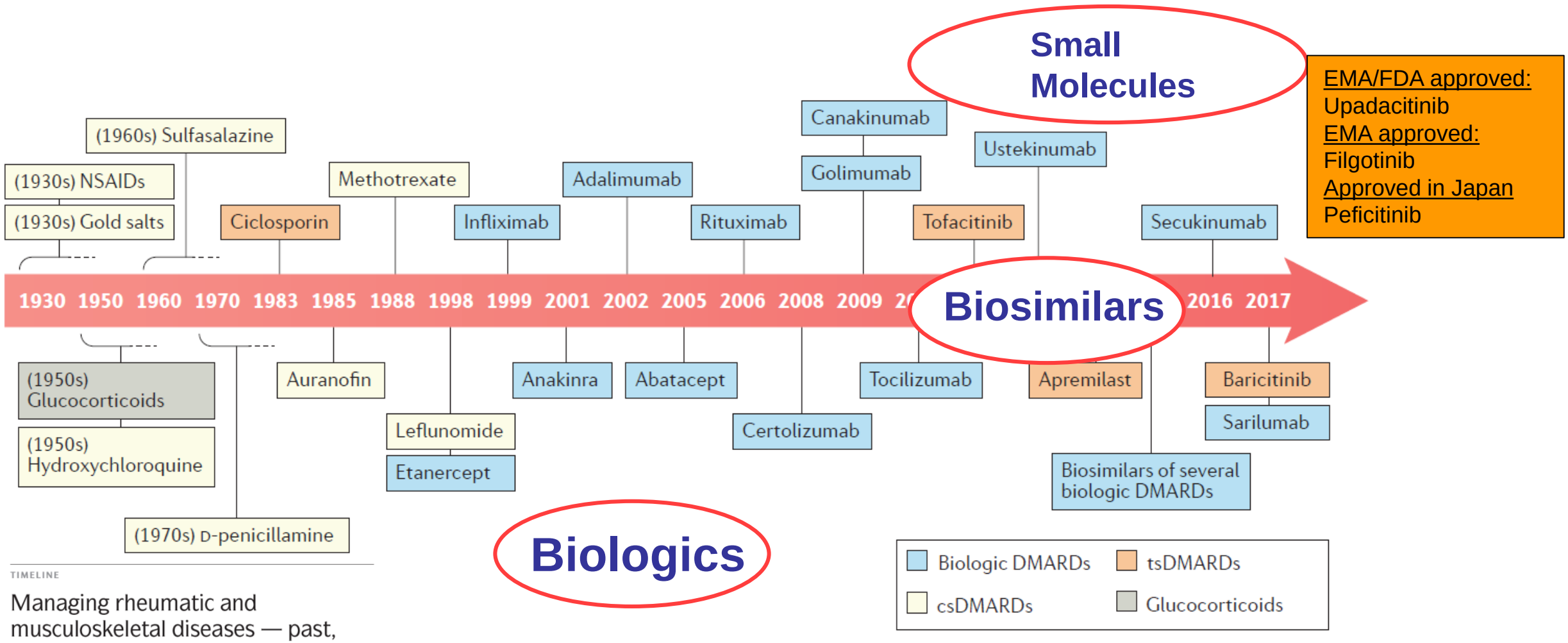
V Furer*, C Rondaan*, M W Heijstek*, N Agmon-Levin, S van Assen, M Bijl, R D'Amelio, M Dougados, M C Kapetanovic, J M van Laar, A Ladefoged de Thurah,A Molto, U Muller-Ladner, K Schreiber, J Walker, N M Wulffraat, **O Elkayam**

Disclosures

- Pfizer, Novartis, Sanofi, Lilly, Abbvie. Janssen

Tel-Aviv Sourasky Medical Center

(R)evolution in the Treatment of Rheumatic Diseases



TIMELINE

Managing rheumatic and musculoskeletal diseases — past, present and future

Gerd R. Burmester, Johannes W. J. Bijlsma, Maurizio Cutolo and Iain B. McInnes

NATURE REVIEWS | RHEUMATOLOGY 2017

Increased risk of infections in patients with rheumatic diseases

- The most common sites of infection :
  - respiratory tract (including pneumonia)
  - skin and soft tissue
  - urinary tract
  - Herpes zoster
  - HPV, mainly in SLE patients

Low uptake of vaccination

- COMORA cohort , 3920 RA patients over 17 countries
- Uptake of pneumococcal vaccination : 17.2%
  - From 0% in Morocco to 56 % in France
- Uptake of influenza vaccination : 25.3%
  - Less than 1% in Morocco to 66 % in Japan

Hmamouch I, Vaccine 2015 ;33(12):1446

EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

S van Assen,[1] N Agmon-Levin,[2] O Elkayam,[3,4] R Cervera,[5] M F Doran,[6] M Dougados,[7] P Emery,[8,9] P Geborek,[10] J P A Ioannidis,[11–14] D R W Jayne,[15] C G M Kallenberg,[16] U Müller-Ladner,[17] Y Shoenfeld,[2,4] L Stojanovich,[18] G Valesini,[19] N M Wulffraat,[20] M Bijl[12]

Ann Rheum Dis 2011;**70**:414–422.

2019 update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

Victoria Furer ,[1,2] Christien Rondaan,[3,4] Marloes W Heijstek,[5] Nancy Agmon-Levin ,[2,6] Sander van Assen,[7] Marc Bijl,[8] Ferry C Breedveld,[9] Raffaele D'Amelio,[10] Maxime Dougados ,[11] Meliha Crnkic Kapetanovic ,[12] Jacob M van Laar ,[13] A de Thurah ,[14] Robert BM Landewé ,[15,16] Anna Molto ,[11] Ulf Müller-Ladner,[17] Karen Schreiber,[18,19] Leo Smolar,[20] Jim Walker,[21] Klaus Warnatz,[22] Nico M Wulffraat ,[23] Ori Elkayam [1,2]

Ann Rheum Dis 2020;**79**:39–52. doi:10.1136/annrheumdis-2019-215882

The task force

- Representatives of 10 European countries
  - 8 adult rheumatologists, 2 clinical immunologists, 1 infectious disease specialist, 2 pediatrician/rheumatologist, 2 delegates of EMEUNET, one health professional in rheumatology, and 2 patients
- Steering committee
  - Convenor, co-convenor, methodologist, 3 fellows, 1 rheumatologist,

  1 infectious diseases

Key points questions for systemic literature review

- New evidence of prevalence of vaccine preventable diseases in patients with rheumatic diseases (SLR question 1)
- Updating on specific vaccines in patients with rheumatic diseases (efficacy and safety) (SLR question 2)
- Effect of DMARDs on the efficacy and safety of vaccination (SLR question 3)
- Stratification of risk of specific infections in predefined groups (SLR question 1)
- Recommendations for vaccination of the population close to patients suffering from AIIRD (SLR question 2)

Definition of AIIRD and immunomodulating agents

- AIIRD
  - RA, JIA, SLE, APS, Still, SS, Sjogren, MCTD, RP, GCA, PMR, Takayasu, AAV, PAN, Behcet, anti-GBM, Cryo, PM/DM,PsA, SpA, Periodic synd.

- Immunomodulating agents
  - GC, MTX, SSZ, Leflunomide, HCQ, Azathioprine, MMF, Tacrolimus, cyclophosphamide, TNFa blockers, rituximab, abatacept, tocilizumab, sarilumab, belimumab, ustekinumab, secukinumab, ixekizumab, apremilast, anti IL1,tofacitinib, baricitinib

Definition of vaccines

- **Inactivated**
  - Diphtheria, hepatitis A, hepatitis B, Haemophilus influenzae b, human papillomavirus, influenza, Neisseria meningitides, pertussis, parenteral poliomyelitis, *streptococcus pneumoniae* (polysaccharide and conjugated), tetanus toxoid, tick-borne encephalitis, parenteral typhoid fever
- **Live-attenuated**
  - Measles, mumps, oral poliomyelitis, oral typhoid fever, varicella zoster, yellow fever

Definition of outcomes

- **Efficacy** : the capacity of vaccinations to prevent infection
- **Immunogenicity** : the capacity of vaccines to induce humoral and cellular immune responses
- For some vaccines, these in vitro immune responses may not correlate well with clinical effectiveness, whereas for other vaccines the correlation is very strong
- **Safety** of vaccines

6 Overarching principles

1.The vaccination status and indications for further vaccination in patients with AIIRD should be assessed yearly by the rheumatology team.

- 2011 : "***initial work up***" vs "***annual assessment***"
- Specialist :
  - extended knowledge and expertise encompassing all aspects of the AIIRD
  - The only treating physician
  - an inventory of vaccinations history, adverse events, and flares of the underlying AIIRD following earlier vaccinations

- Implementation of this recommendation may increase the uptake of vaccinations among patients with AIIRD

2.The individualized vaccination program should be explained to the patient providing a basis for informed decision and then be implemented jointly by the treating specialist, primary care physician and the patient

- Newly formulated principle
- Strongly endorsed by the patients representatives
- Shared decision-making and consideration of patient's needs

3. Vaccination in AIIRD patients should preferably be administered during quiescent disease

- Most vaccination studies conducted in the AIIRD population included patients with quiescent disease
- Juvenile SLE with high SLE activity had reduced seroconversion rates to influenza A H1N1 vaccination
- 340 RA patients, including patients with moderate to severe disease activity, did *not* show a significant difference in side effects, disease flares or level of sero-protection following influenza A H1N1 vaccination in patients with active disease

Arthritis care & research. 2013;65(7):1121-7.

Annals of the rheumatic diseases. 2011;70(12):2144-7.

4.Vaccines should be preferably administered prior to planned immunosuppression, in particular B cell depleting therapy

	Influenza	PVP23
MTX	−	−
TNF a Blockers	+	−
Tocilizumab	+	+
Abatacept	+ −	+ −
Tofacitinib	+	−
Rituximab	− −	− −
High dose GC, IS	−	−

5.Non-live vaccines can be administered to AIIRD patients during the use of corticosteroids and disease modifying anti-rheumatic drugs (DMARDs)

- Influenza, pneumococcal, hepatitis B (HCV), tetanus toxoid, and Haemophilus influenzae b, and hepatitis A (HAV) vaccines to patients with AIIRD under immuno-modulating therapy
- Satisfactory immuno-protection in the majority of studies
- No major safety signals
- Follow up period was mainly short-term

6. Live-attenuated vaccines may be considered with caution in patients with AIIRD

- 2011.***Live attenuated vaccines should be avoided in immunosuppressed AIIRD patients, with the possible exceptions of herpes zoster and measles, mumps, rubella (MMR)***
- The preferable window time for the vaccination with live vaccines is 4 weeks prior to treatment initiation
- MMR, varicella, and herpes zoster vaccines may be an exception
- Evidence from children on the immunogenicity and safety of MMR , in pts treated with MTX and even biologics
- Measles virus booster vaccine can be considered in AIIRD patients at risk of contracting measles infection
- Varicella may be considered
  - Good safety reported in JIA and other pediatric CTD

Recommendations

1 .*Influenza vaccination should be strongly considered for the majority of patients with AIIRD*

- Evidence on efficacy and immunogenecity
  - Studied in RA, SLE, AAV, SSc, PsA
  - cDMARDs, TNF a blockers, tocilizumab, tofacitinib, rituximab, abatacept
- Most studies focused on immunogenicity
- Temporary discontinuation of MTX may improve response
- Increased dose of the vaccine or a second booster may improve response in naïve patients

Types of flu vaccines

- Inactivated vaccines
  - Trivalent flu vaccine
  - Quadrivalent flu vaccine
  - High dose vaccine

- Live attenuated vaccine
  - Nasal spray vaccine (age: 2-49y)

2. *Pneumococcal vaccination should be strongly considered for the majority of patients with AIIRD*

- Increased risk for pneumococcal disease
- Efficacy of PVP-23
  - RCT did not demonstrate efficacy of PVP23 over placebo
  - Retrospective study showed a RR of 9.7 for developing pneumonia among non-vaccinated patients
- Immunogenicity
  - PVP23 : Many studies in RA, SLE, JIA, PSA
  - PCV13 and PVP 23 : 1 study in RA pts with good response
  - PCV13 : reduced in SLE, not affected by belimumab
- Safety
  - No significant safety issue
  - Severe local reactions to PVP 23 in CAPS (Cryopyrin-Associated Autoiinflammatory syndrome)

Pneumococcal vaccination

- Stepwise pneumococcal vaccination, a PCV13 prime-PPSV23 boost strategy, with an interval of at least 8 weeks between the two vaccinations, is now recommended based on the CDC and the European Society of Clinical Microbiology and Infectious Diseases

3. **Patients with AIIRD should receive tetanus toxoid vaccination in accordance to recommendations for the general population. Passive immunization should be considered for patients treated with B cell depleting therapy.**

- No studies on infections rates
- Good correlation between Ab concentration and infection
- Good immunogenicity demonstrated in RA and SLE
- A single dose every 10 years

4. *Hepatitis A and B vaccines can be administered to AIIRD patients at risk*

- No efficacy data
- Good correlation with Ab levels
- Good immunogenicity
- As opposed to strong immunogenicity in healthy individuals, a single dose of HAV vaccine does not provide a sufficient protection in RA and patients using immunosuppressive drugs. Second HAV vaccination after 6 months and determination of post-vaccination antibody titers is recommended
- **Patients at risk :**
  - seronegative AIIRD patients that travel to or are residents of endemic countries
  - increased risk of exposure to hepatitis B (medical profession, infected family member or contacts, injecting drug users, men who have sex with men)

5. *Herpes zoster vaccination may be considered in high-risk patients with AIIRD*

- Increased risk to develop HZ
- A live attenuated vaccine reduces HZ risk by 51-70% among healthy individuals > 50 y old
- In AIIRD patients, vaccination with live attenuated zoster vaccine was associated with a reduced incidence of herpes zoster in patients over 60 years (retrospective database , RA, PsA, AS, psoriasis, IBD)
- Safe , including when administered 2 weeks before tofacitinib
- Perform varicella antibodies in patients with uncertain varicella exposure
- Non-live recombinant subunit adjuvant zoster vaccine may be a game changer

6. Vaccination against yellow fever should be generally avoided in patients with AIIRD

- This is a newly formulated recommendation.
- The rationale for specifically addressing the yellow fever vaccine stems from the fact that travelling to the endemic area for yellow fever in the South America and Africa has become popular in the European countries
- The yellow fever vaccine is a live-attenuated vaccine. A single dose of which is sufficient to confer sustained immunity against yellow fever disease

7. Patients with AIIRD, in particular patients with SLE, should receive vaccinations against HPV in accordance with recommendations for the general population

- Increased rate of HPV infection and cervical dysplasia in SLE pts
- Variables associated with HPV infections in SLE
  - Multiple sexual partners, STD, younger age
- No efficacy data
- Good immunogenicity data
- Safety
  - Controversial results on flares after vaccination, case reports on onset of SLE
- **Patients at risk :**
  - young SLE patients on immunosuppressive therapy, multiple sexual partners, previous HPV infection, or previous STD

8. Immunocompetent household members of patients with AIIRD should be encouraged to receive vaccines according to national guidelines with the exception of the oral polio vaccine

- Expert opinion
- Household members of immunosuppressed patients, should receive inactivated vaccines as well as live attenuated vaccines such as MMR, rotavirus, varicella and zoster vaccine, according to national guidelines
- Oral polio vaccine should be avoided
- Avoid handling with diapers of infants vaccinated against rotavirus in highly immunocompromised patients
- Avoid contact with persons developing skin lesions after varicella or zoster vaccines

9. Live attenuated vaccines should be avoided during the first 6 months of life in newborns of mothers treated with biologics during the second half of pregnancy

- Since IgG crosses the placenta during the third trimester, biologics are detectable in newborns of mothers treated with biologics until approximately 6 months
- A fatal case of disseminated TB in a newborn exposed to biologics

What is new in this update ?

- Responsibility of the specialist
- Shared patient decision
- Pneumococcal vaccines
- More flexible approach to certain live attenuated vaccines
- Household members and newborns

COVID-19 VACCINES

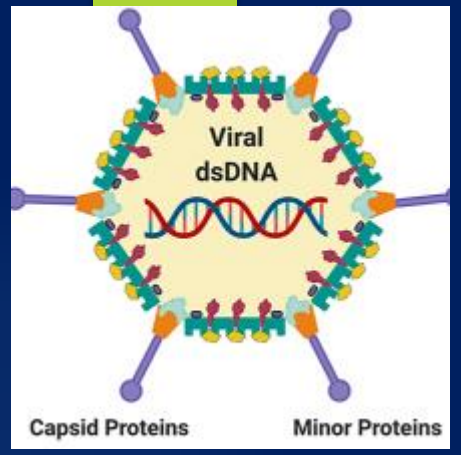
COVID19 VACCINES

RNA vaccines

- BNT162b2 (Pfizer)
- mRNA-1273 (Moderna)

Adenovirus based vaccines

- ChAdOx1 nCoV-19 (Astrazeneca)
- Ad26.COV2-S (Janssen)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 31, 2020 VOL. 383 NO. 27

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

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 2021; 397: 99–111

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

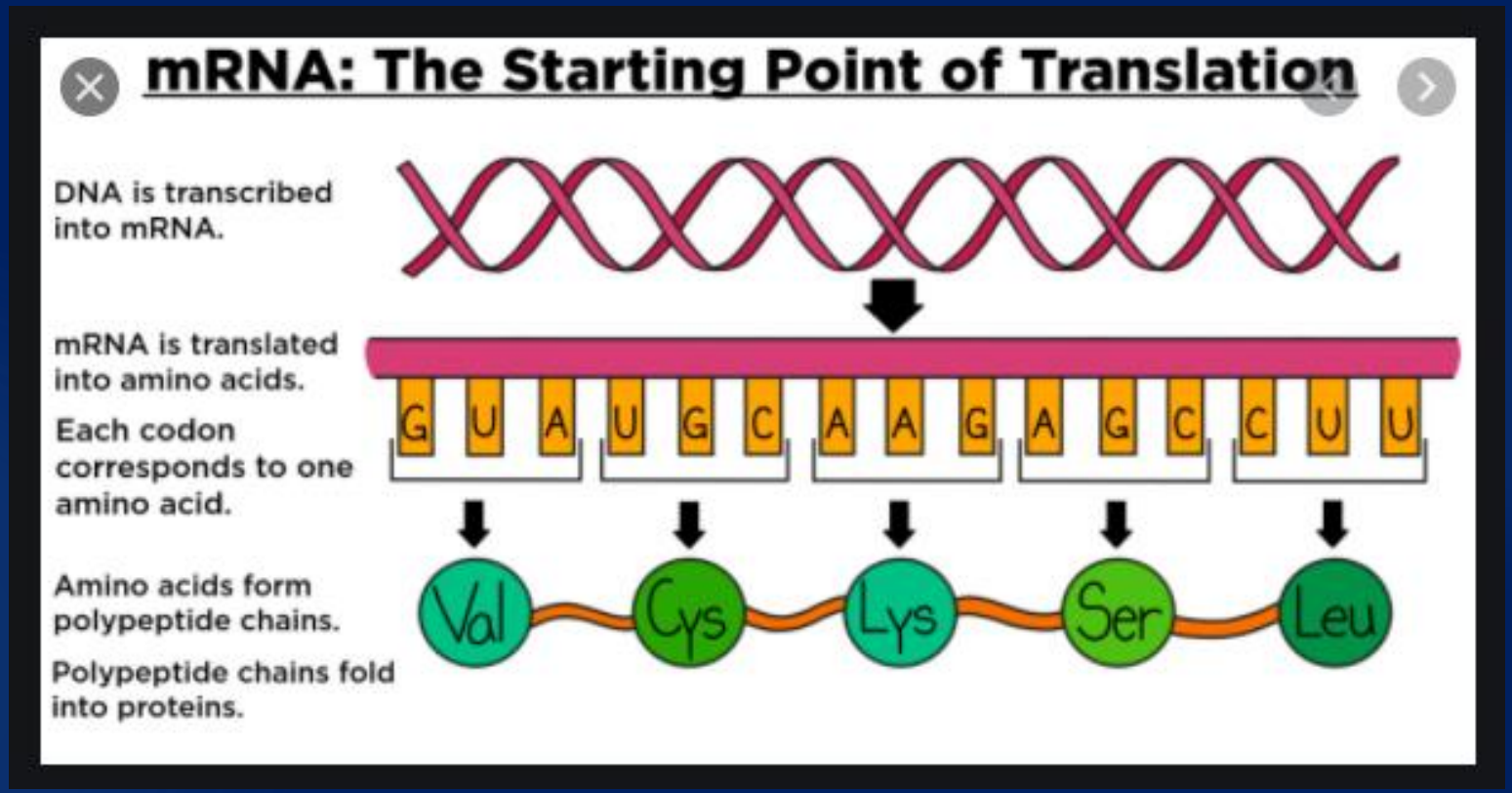
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

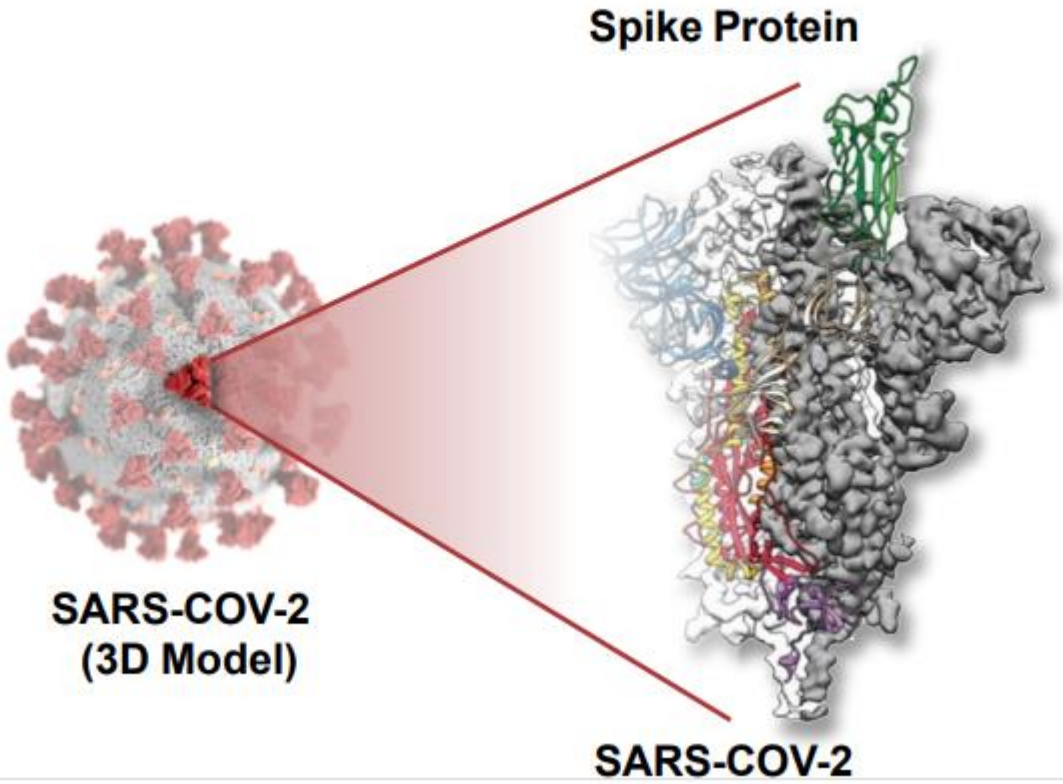
Interim Results of a Phase 1–2a Trial of Ad26.COV2.S Covid-19 Vaccine

BNT162b2 Vaccine Candidate Against COVID-19

Vaccines and Related Biological Products Advisory Committee


mRNA: The Starting Point of Translation
DNA is transcribed into mRNA.
mRNA is translated into amino acids.
Each codon corresponds to one amino acid.
Amino acids form polypeptide chains.
Polypeptide chains fold into proteins.
G U A U G C A A G A G C C U U
Val
Cys
Lys
Ser
Leu

Importance of SARS-COV-2 Spike Protein



Advantages of mRNA Vaccine Platform

Safety

Non-infectious, chemically defined, no viral foreign proteins

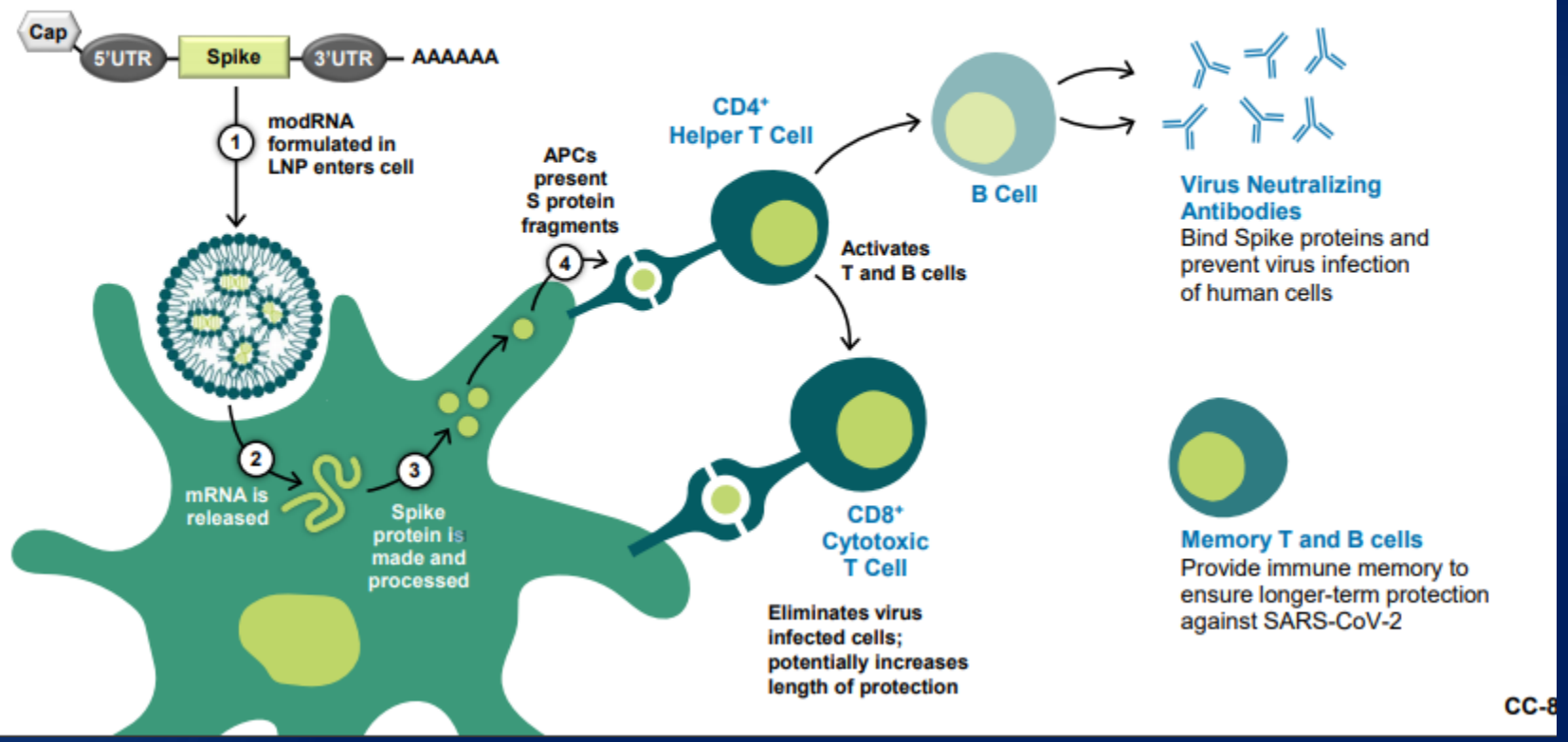
Efficacy

Broad immune responses, minimal risk of anti-vector immunity, and permits **frequent boosting**

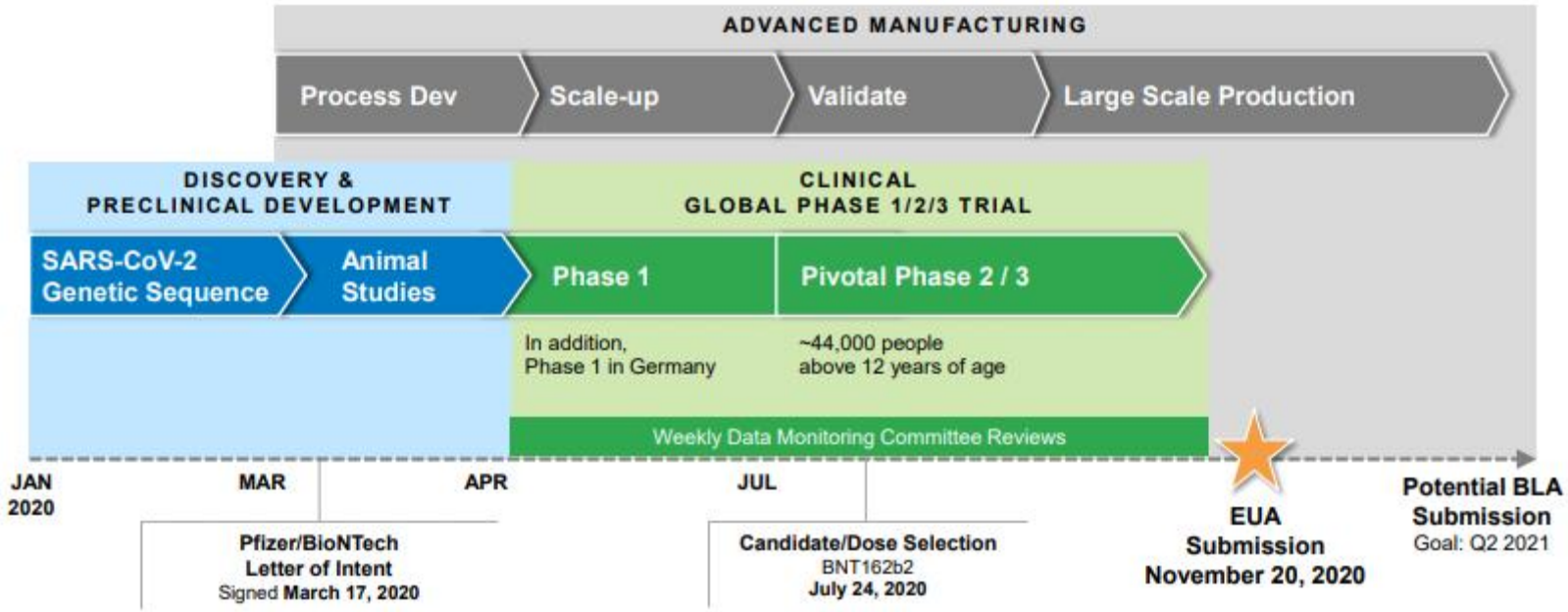
Rapid Response

Technology enables **rapid development** and **quick production scaling**

Mode of Action of the BNT162 Vaccine Candidates



Responding to the Global Health Crisis with the BNT162b2 Vaccine



Efficacy & Safety Topics

- **Phase 1 German and US studies**
  - Safety
  - Immunogenicity
- **Phase 2/3 global study**
  - Study design
  - Primary/secondary objectives
  - COVID-19 definitions
  - Safety
  - Efficacy

Planned Subjects in Pivotal Study

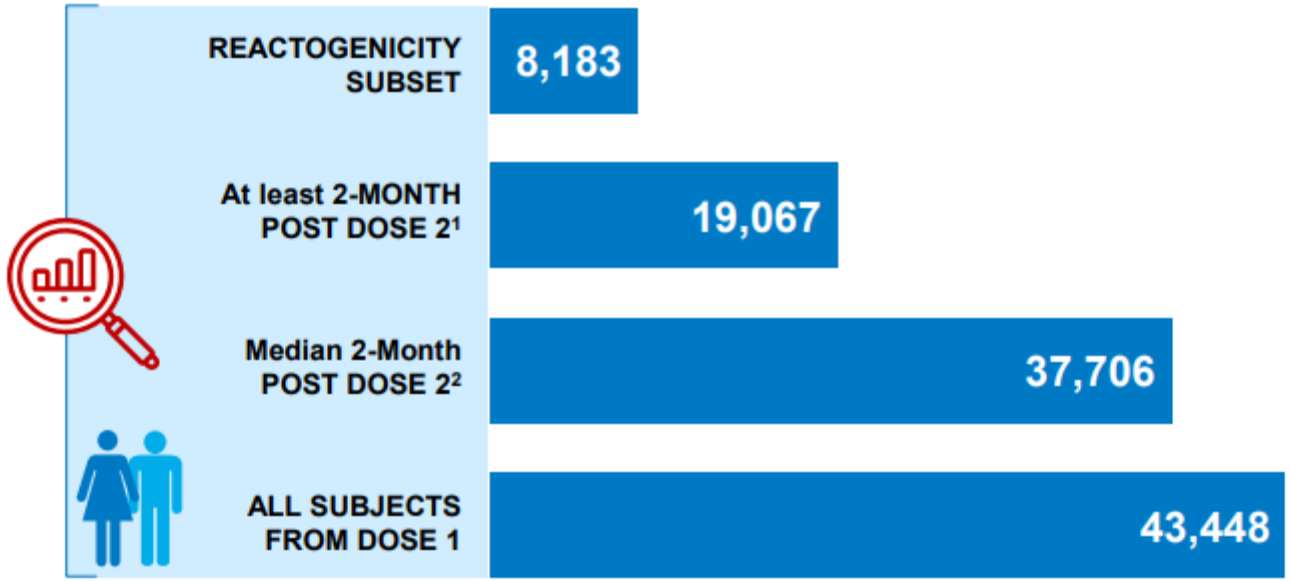
- **44,000 healthy subjects enrollment target**
  - Stable chronic disease allowed
  - Stable HIV, HBV, HCV
- **At least 40% ages 56 years or older**
- **Balanced racial and ethnicity profile**
  - Black/African American
  - Asian
  - Hispanic/Latinx
- **Immunocompromised excluded**

Demographic Characteristics
Phase 2/3 (N=43,448)

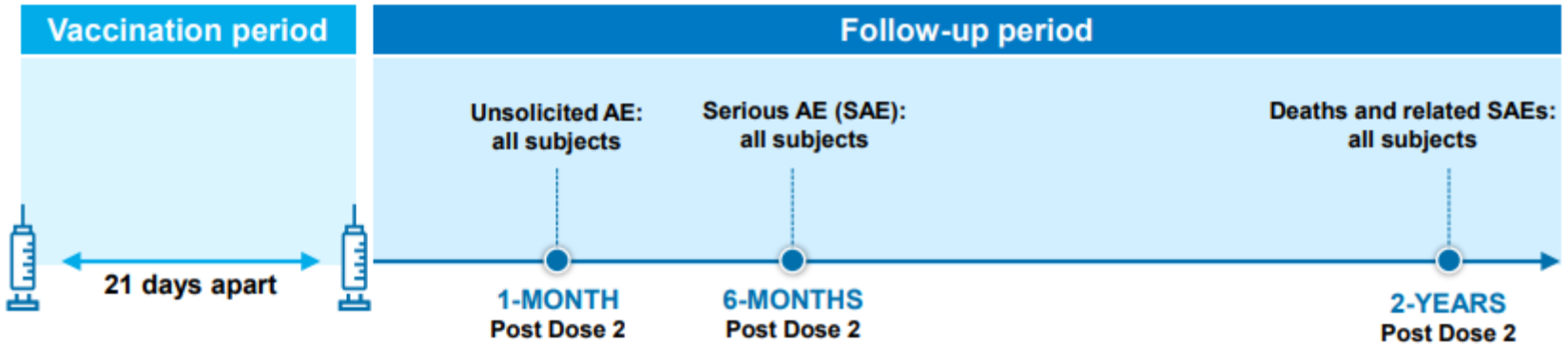
		BNT162b2 (30 µg) N=21,720 n (%)	Placebo N=21,728 N (%)	Total N=43,448 n (%)
Sex	Male	11,183 (51.5)	10,942 (50.4)	22,125 (50.9)
	Female	10,537 (48.5)	10,786 (49.6)	21,323 (49.1)
Race	White	17,839 (82.1)	17,857 (82.2)	35,696 (82.2)
	Black or African American	2,091 (9.6)	2,107 (9.7)	4,198 (9.7)
	All others	1,790 (8.2)	1,764 (8.1)	3,554 (8.2)
Ethnicity	Hispanic/Latino	5,672 (26.1)	5,668 (26.1)	11,340 (26.1)
	Non-Hispanic/non-Latino	15,928 (73.3)	15,940 (73.4)	31,868 (73.3)
	Not reported	120 (0.6)	120 (0.6)	240 (0.6)
Age	16-55 Years	12,780 (58.8)	12,822 (59.0)	25,602 (58.9)
	>55 Years	8,940 (41.2)	8,906 (41.0)	17,846 (41.1)
	16-64 Years	17,176 (79.1)	17,190 (79.1)	34,366 (79.1)
	65-74 Years	3,620 (16.7)	3,646 (16.8)	7,266 (16.7)
	≥75 Years	924 (4.3)	892 (4.1)	1,816 (4.2)

>9000 (20.9%)

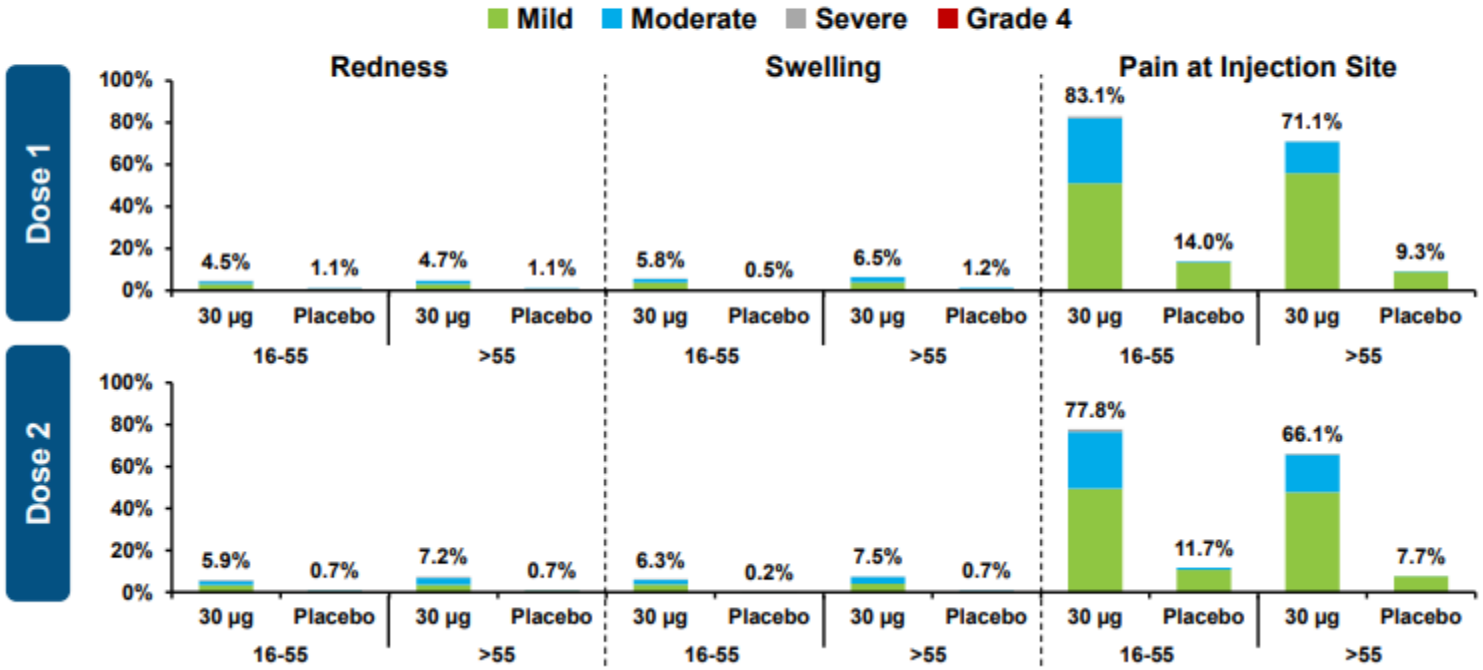
Summary of Safety Data



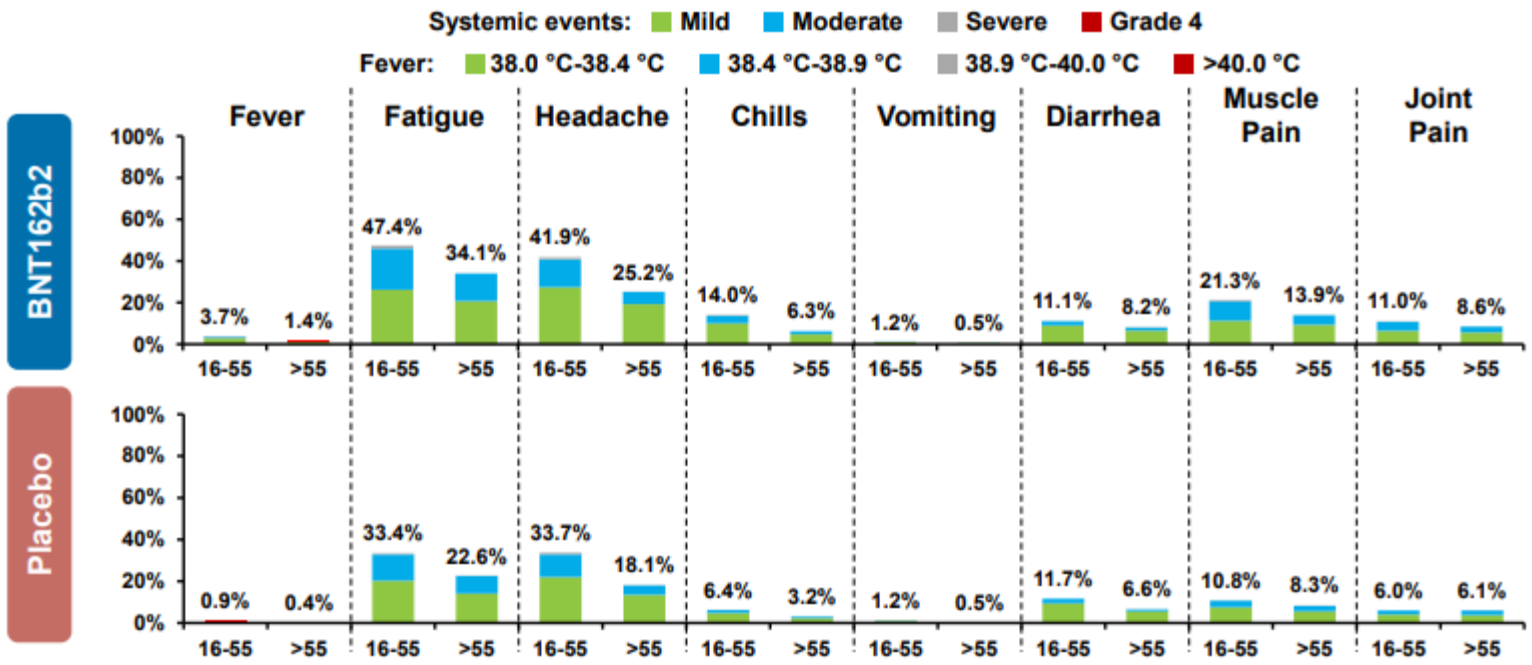
Phase 2/3 Safety – Study Start 27 July, 2020



eDiary: Local Events Within 7 Days From Dose 1 and 2 in 16-55 and >55 Year Olds (N=8,183)

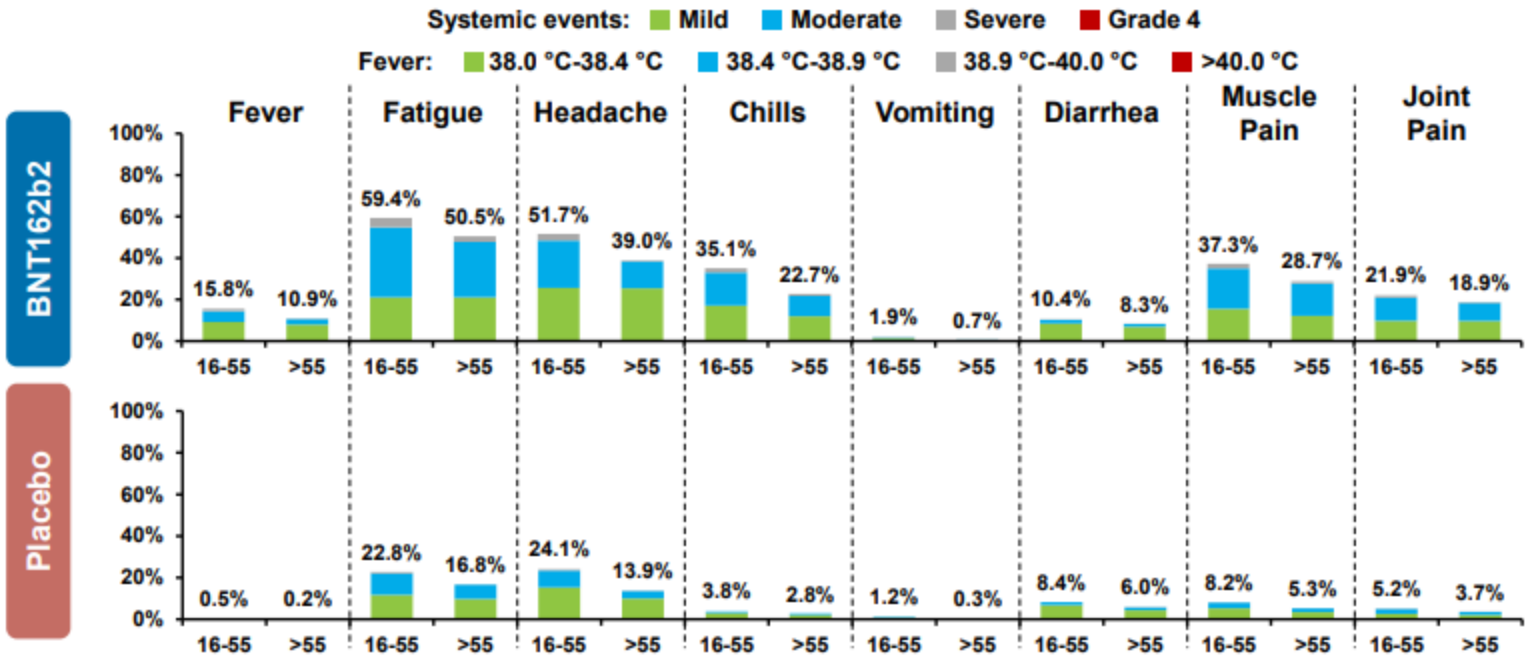


eDiary: Systemic Events Within 7 Days From Dose 1 in 16-55 and >55 Year Olds (N=8,183)



Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization

eDiary: Systemic Events Within 7 Days From Dose 2 in 16-55 and >55 Year Olds (N=8,183)



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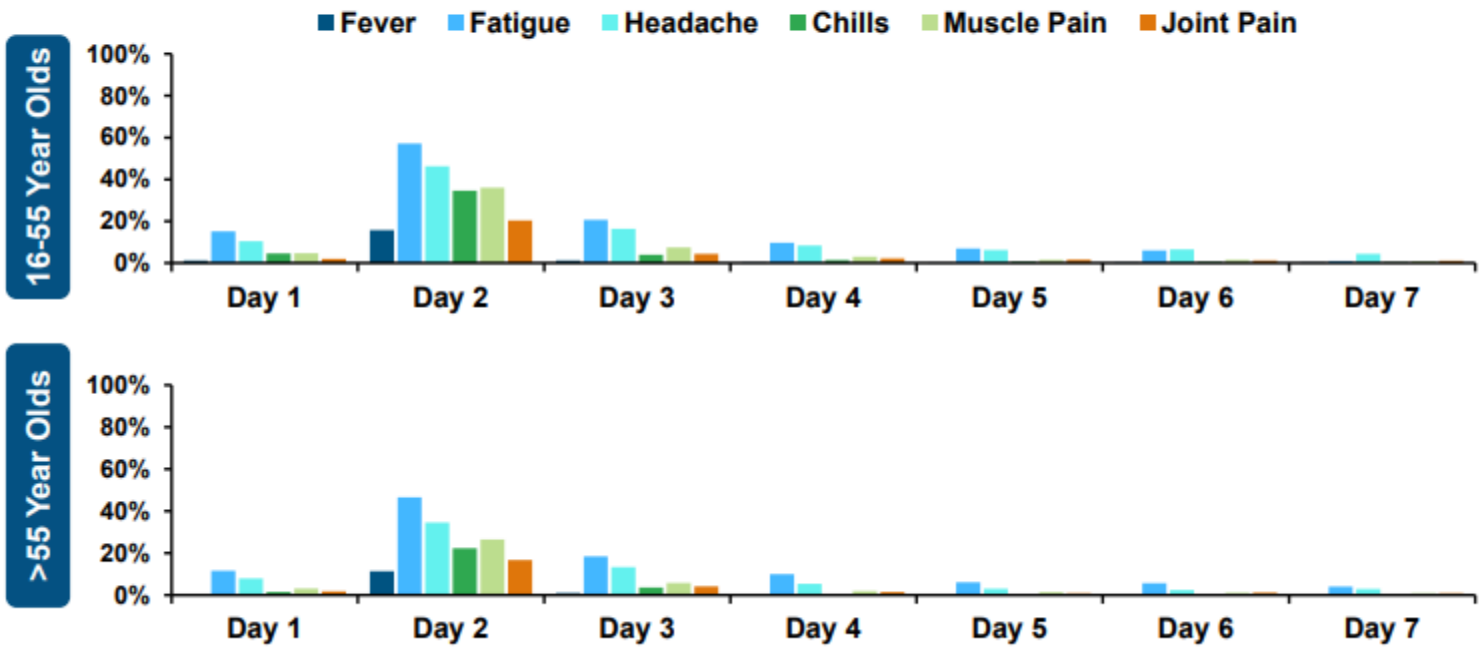
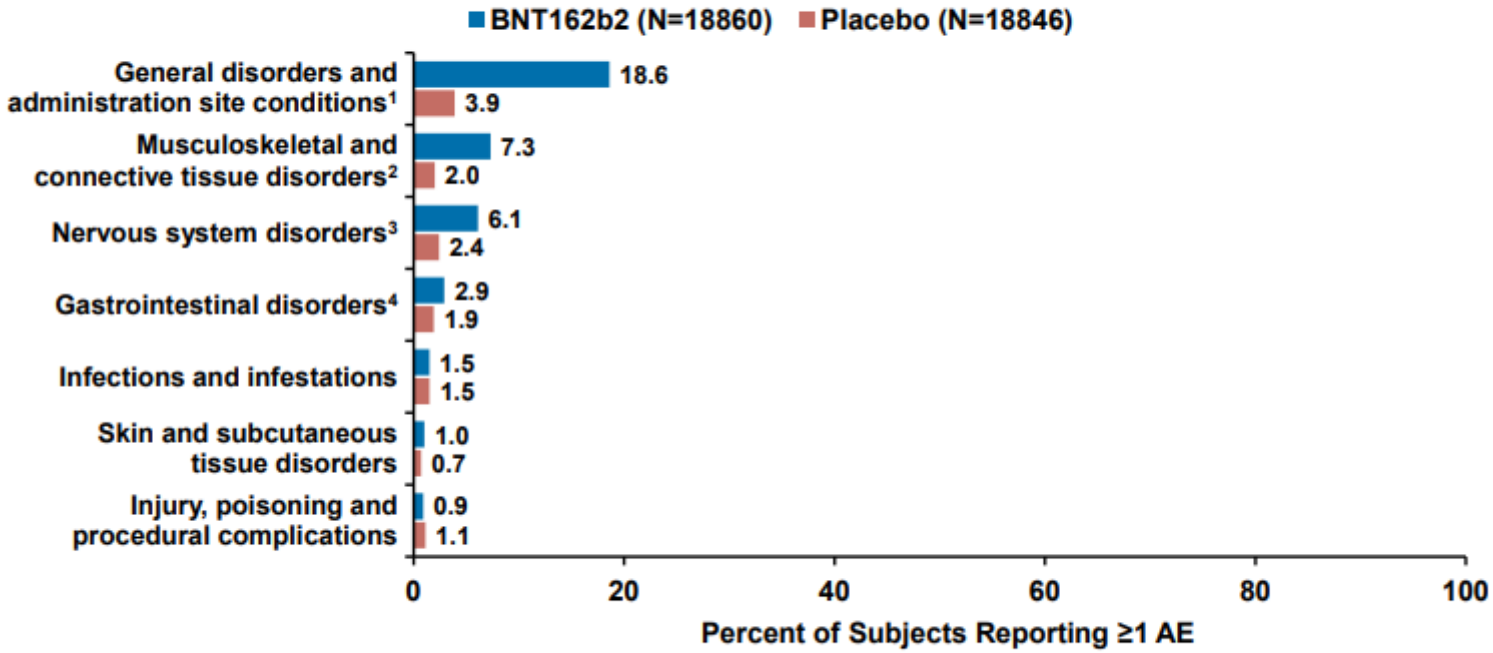
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization

eDiary: Systemic Events Each Day From Dose 2 in 16-55 and >55 Year Olds (N=8,183) BNT162b2



Adverse Events ≥1.0% by System Organ Class

~50% of Subjects with Mean of 2 Months Post Dose 2 (N=37,706)



1. Predominantly reflect local reactions at the injection site and systemic reactions of fatigue and chills
2. Predominantly reflect myalgias and arthralgia's as part of systemic events
3. Predominantly reflects Headache
4. Predominantly reflects diarrhea and vomiting

CC-32

Serious Adverse Events by System Organ Class ≥0.1%
All Enrolled Subjects (N=43,448)

	BNT162b2 (30 µg) N=21,720 n (%)	Placebo N=21,728 n (%)
Any event	126 (0.6)	111 (0.5)
Infections and infestations	27 (0.1)	17 (0.1)
Cardiac disorders	18 (0.1)	18 (0.1)
Nervous system disorders	18 (0.1)	16 (0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	11 (0.1)	8 (0.0)
Injury, poisoning and procedural complications	8 (0.0)	12 (0.1)

Deaths

All Enrolled Subjects (N=43,448)

	BNT162b2 (30 µg) N=21,720 n (%)	Placebo N=21,728 n (%)
Deaths	2 (0.0)	4 (0.0)

Summary of Safety Analyses Available

EUA	BLA
Reactogenicity in ~8,000 total	Reactogenicity >8,000 total
AE/SAE assessed in 37,706 total with median 2 month follow-up post dose 2	AE/SAE assessed in ~44,000 total with at least 6000 participants with 6 month or more post dose 2
AE/SAE in 43,448 total in age 16 years and above	Reactogenicity and AE/SAE in 12-15 year old cohort

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy – Final Analysis

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

	BNT162b2 (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

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy – Final Analysis: Subgroups

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

		BNT162b2 N=18,198 n	Placebo N=18,325 n	VE (%)	(95% CI)
Overall		8	162	95.0	(90.0, 97.9)
Age	18-64 years	7	143	95.1	(89.6, 98.1)
	65-74 years	1	14	92.9	(53.1, 99.8)
	≥75 years	0	5	100.0	(-13.1, 100.0)
Sex	Male	3	81	96.4	(88.9, 99.3)
	Female	5	81	93.7	(84.7, 98.0)
Race	White	7	146	95.2	(89.8, 98.1)
	Black or African American	0	7	100.0	(31.2, 100.0)
	All Others	1	9	89.3	(22.6, 99.8)
Ethnicity	Hispanic/Latino	3	53	94.4	(82.7, 98.9)
	Non-Hispanic/Non-Latino	5	109	95.4	(88.9, 98.5)
Country	Argentina	1	35	97.2	(83.3, 99.9)
	Brazil	1	8	87.7	(8.1, 99.7)
	USA	6	119	94.9	(88.6, 98.2)

First COVID-19 Occurrence From 7 Days After Dose 2 by Comorbidity Status – Evaluable Efficacy (7 Days) Population

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

	BNT162b2 (30 µg) N=18,198		Placebo N=18,325			
	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
Overall	8	2.214 (17,411)	162	2.222 (17,511)	95.0	(90.0, 97.9)
Comorbidity						
No comorbidity	4		76		94.7	(85.9, 98.6)
Any comorbidity	4		86		95.3	(87.7, 98.8)
Any malignancy	1		4		75.7	(-145.8, 99.5)
Cardiovascular	0		5		100.0	(-0.8, 100.0)
Chronic pulmonary disease	1		14		93.0	(54.1, 99.8)
Diabetes	1		19		94.7	(66.8, 99.9)
Obese (≥30.0 kg/m^2)	3		67		95.4	(86.0, 99.1)
Hypertension	2		44		95.4	(82.6, 99.5)
Diabetes (including gestational diabetes)	1		20		95.0	(68.7, 99.9)

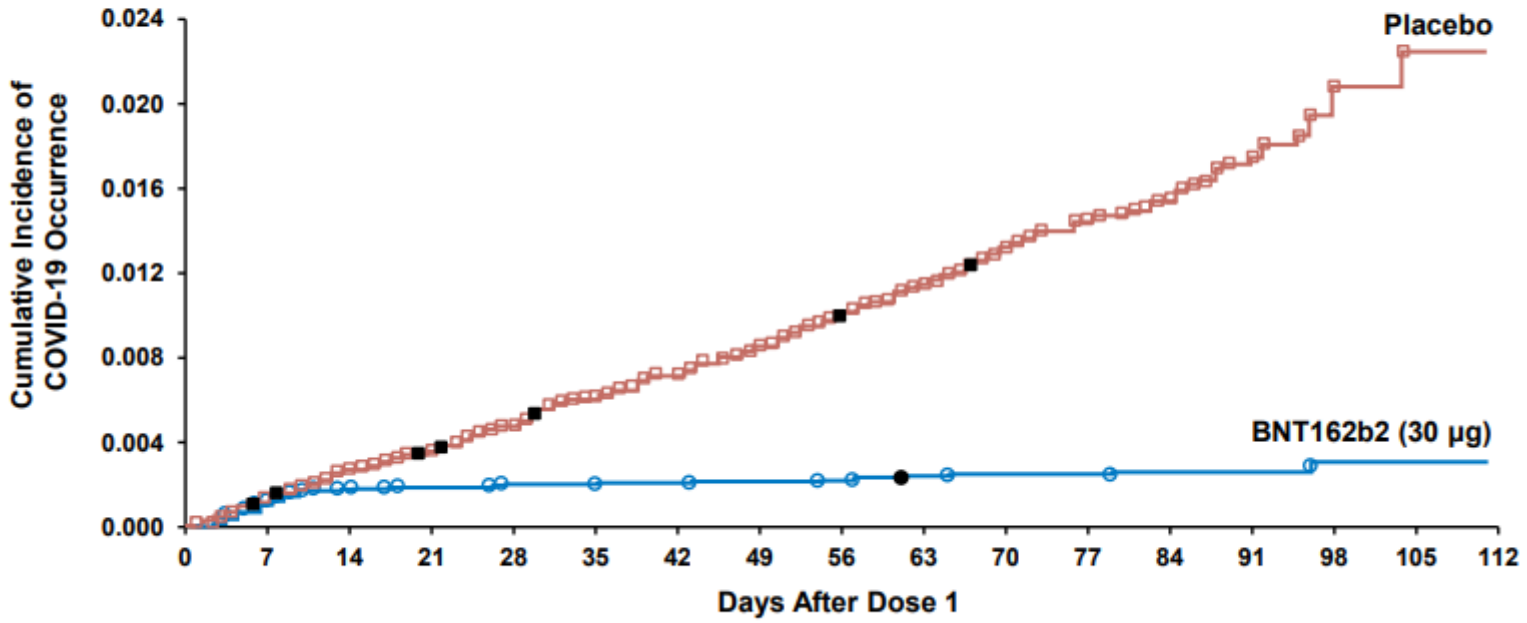
BNT162b2 Protects Against Severe Disease

Phase 2/3 Efficacy – Final Analysis (FDA Definition)

	BNT162b2 (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 Severe COVID-19 occurrence ≥7 days after Dose 2	1	2.215 (17,411)	3	2.232 (17,511)	66.4	(-124.8, 96.3)	0.7429

	BNT162b2 (30 µg) N=21,669		Placebo N=21,686			
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
First Severe COVID-19 occurrence after Dose 1	1	4.021 (21,314)	9	4.006 (21,259)	88.9	(20.1, 99.7)

Cumulative Incidence of COVID-19 After Dose 1

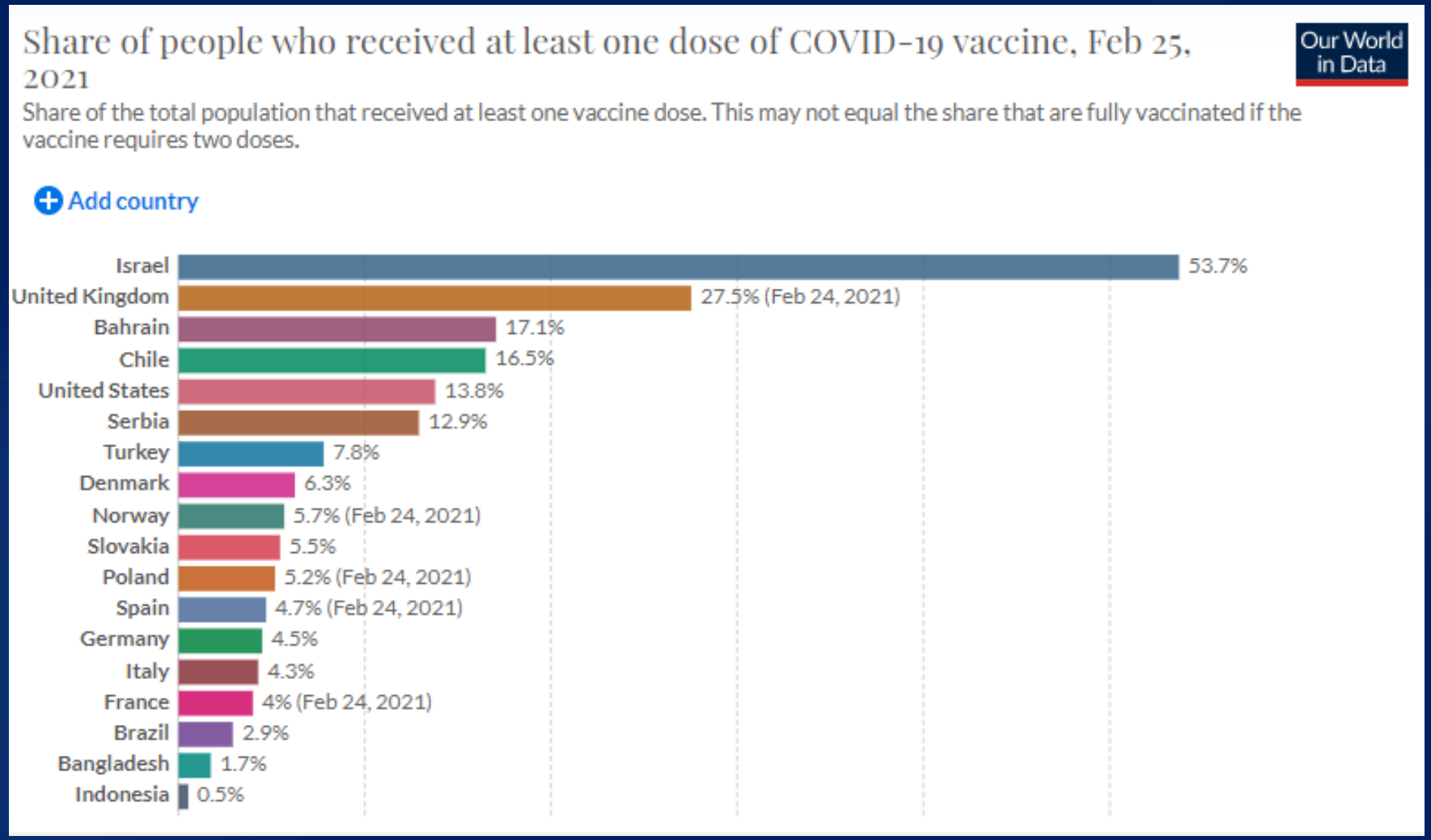


First COVID-19 Occurrence After Dose 1

	BNT162b2 (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)

Efficacy Conclusions

- Both primary objectives met success criteria
- In individuals without prior SARS-CoV-2 infection, observed Vaccine efficacy against COVID-19 occurring at least 7 days after Dose 2 was 95%, with high probability (97.5%) that the true vaccine efficacy is at least 90%
- Observed Vaccine Efficacy was >93% for the first primary endpoint across age, race, ethnicity, and at-risk subgroups


Share of people who received at least one dose of COVID-19 vaccine, Feb 25, 2021
Our World in Data
Share of the total population that received at least one vaccine dose. This may not equal the share that are fully vaccinated if the vaccine requires two doses.
Add country
Israel 53.7%
United Kingdom 27.5% (Feb 24, 2021)
Bahrain 17.1%
Chile 16.5%
United States 13.8%
Serbia 12.9%
Turkey 7.8%
Denmark 6.3%
Norway 5.7% (Feb 24, 2021)
Slovakia 5.5%
Poland 5.2% (Feb 24, 2021)
Spain 4.7% (Feb 24, 2021)
Germany 4.5%
Italy 4.3%
France 4% (Feb 24, 2021)
Brazil 2.9%
Bangladesh 1.7%
Indonesia 0.5%

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting

Noa Dagan, M.D., Noam Barda, M.D., Eldad Kepten, Ph.D., Oren Miron, M.A., Shay Perchik, M.A., Mark A. Katz, M.D., Miguel A. Hernán, M.D., Marc Lipsitch, D.Phil., Ben Reis, Ph.D., and Ran D. Balicer, M.D.

Methods

- All persons who were newly vaccinated during the period from December 20, 2020, to February 1, 2021, were matched to unvaccinated controls in a 1:1 ratio according to demographic and clinical characteristics.
- Study outcomes included documented infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), symptomatic Covid-19, Covid-19–related hospitalization, severe illness, and death.
- We estimated vaccine effectiveness for each outcome as one minus the risk ratio, using the Kaplan–Meier estimator.

Results

- Each study group included 596,618 persons.
- Estimated vaccine effectiveness for the study outcomes at days 14 through 20 after the second dose :
  - symptomatic illness : 92%
  - hospitalization : 87%
  - severe disease : 92% ,

Conclusions

- BNT162b2 mRNA vaccine is effective for a wide range of Covid-19–related outcomes, a finding consistent with that of the randomized trial.

RMD Open
Rheumatic & Musculoskeletal Diseases

VIEWPOINT

Point of view on the vaccination against COVID-19 in patients with autoimmune inflammatory rheumatic diseases

Victoria Furer ,[1,2] Christien Rondaan ,[3] Nancy Agmon-Levin,[2,4] Sander van Assen,[5] Marc Bijl,[6] Meliha Crnkic Kapetanovic,[7] Annette de Thurah ,[8,9] Ulf Mueller-Ladner,[10] Daphna Paran,[1,2] Karen Schreiber,[11,12] Klaus Warnatz,[13] Nico M Wulffraat,[14] Ori Elkayam[1,2]

Points of considerations regarding COVID-19 vaccine in patients with AIIRD

- 1. The risk of contracting COVID-19 for patients with AIIRD seems to be similar to the general population, or at most, mildly increased.
- 2. For most patients with AIIRD, the course of COVID-19 is similar to the background population and is mainly affected by the presence of the classical risk factors for severe COVID-19
- 3. The course of COVID-19 may be more severe in patients with SLE, APS, pSS, vasculitis and congenital or acquired interferonopathies.
- 4. The use of prednisone at a dosage above 10mg/day, mycophenolate mofetil and rituximab has been associated with worse COVID-19 prognosis.
- 5. In general, non-live vaccines are recommended in patients with AIIRD
- 6. In the midst of the COVID-19 pandemic, vaccination against influenza and streptococcus pneumonia should be highly encouraged

- 7. RNA vaccines against COVID-19 are non-live vaccines and do not provoke COVID-19 infection.
- 8. In view of the COVID-19 pandemic, the possible adverse course of COVID-19 in AIIRD patients and the favourable safety profile of the mRNA vaccines in the general population, mRNA vaccines should be administered to patients with AIIRD as recommended in the general population.
- 9. The same statement is valid for other non-live future vaccines if their efficacy and safety profile is found to be similar to BNTb262 and mRNA-1273 vaccines
- 10. As for other vaccines, the efficacy of a COVID-19 vaccine may be reduced in patients treated with high doses corticosteroids and rituximab. For patients treated with rituximab, it is preferable to administer the vaccine at least 6 months after the last infusion.
- 11. There is an urgent need for studies on the immunogenicity and safety of COVID-19 vaccines in patients with AIIRD


THANK YOU
thanks
THANKS
Thanks
Gracias
THANKS
danke!
謝謝
شكرا
THANK
YOU
gracias
THANK

2019 Update of EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases

V Furer*, C Rondaan*, M W Heijstek*, N Agmon-Levin, S van Assen, M Bijl, R D'Amelio, M Dougados, M C Kapetanovic, J M van Laar, A Ladefoged de Thurah,A Molto, U Muller-Ladner, K Schreiber, J Walker, N M Wulffraat, **O Elkayam**