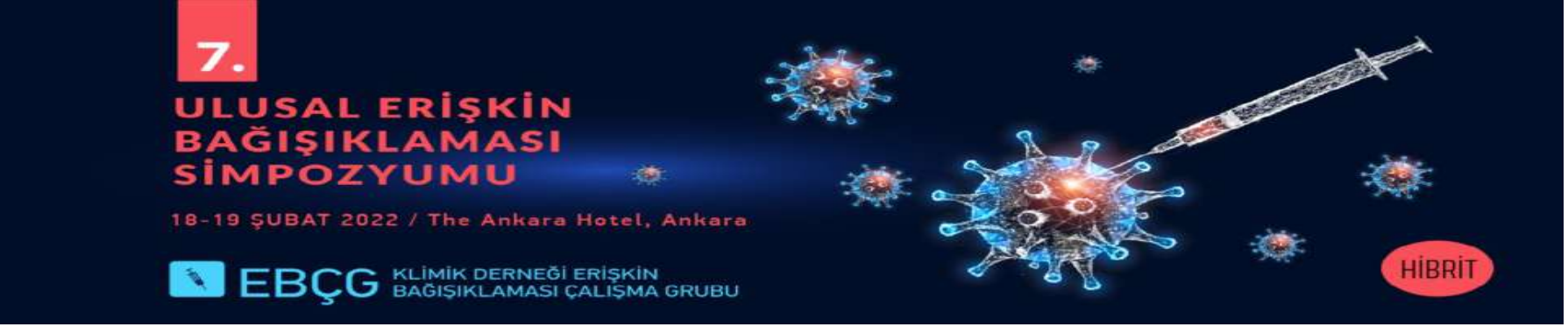


COVID19 BAĞLAMINDA AŞI GELİŞTİRME TEKNOLOJİLERİ

VEKTÖR AŞILARI

Prof.Dr. Ener Çağrı Dinleyici

Eskişehir Osmangazi Üniversitesi Tıp Fakültesi

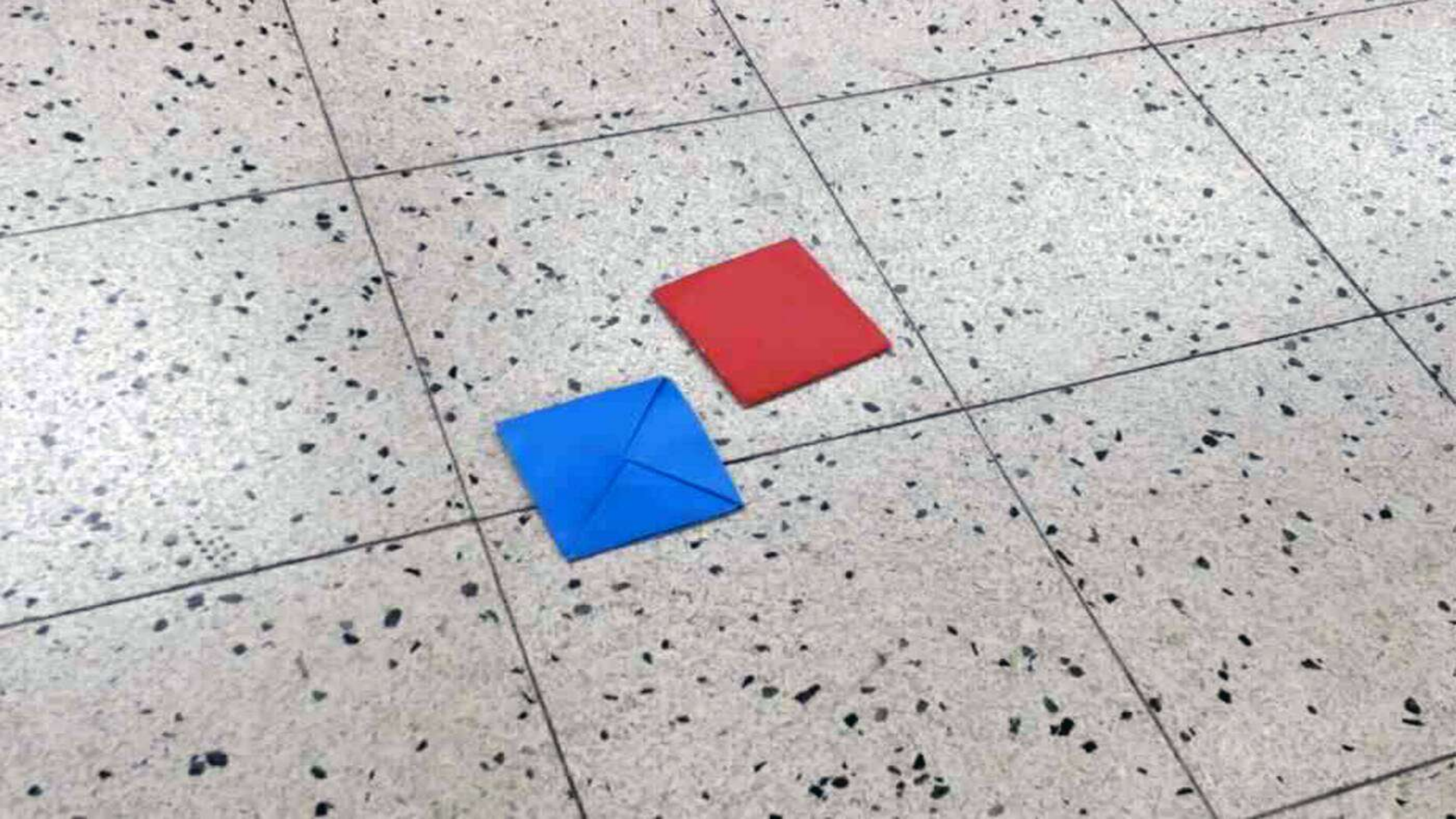
Çocuk Sağlığı ve Hastalıkları Anabilim Dalı

19 Şubat 2022

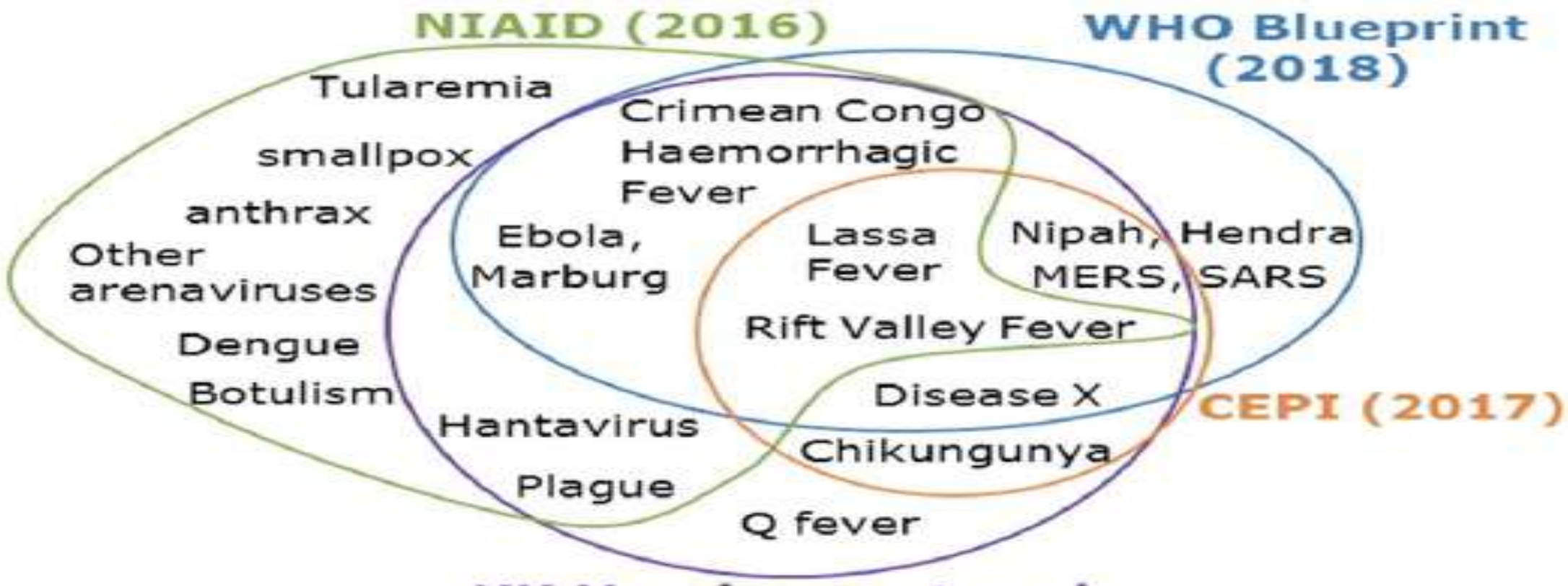
Ulusal Erişkin Bağışıklama Sempozyumu

@timbooth75

@ecdinleyici



SALGIN AŞILAMASI



Noad et al. Vaccine 2019

SALGIN AŞILAMASINDA ADENOVİRÜS VEKTÖRLERİ

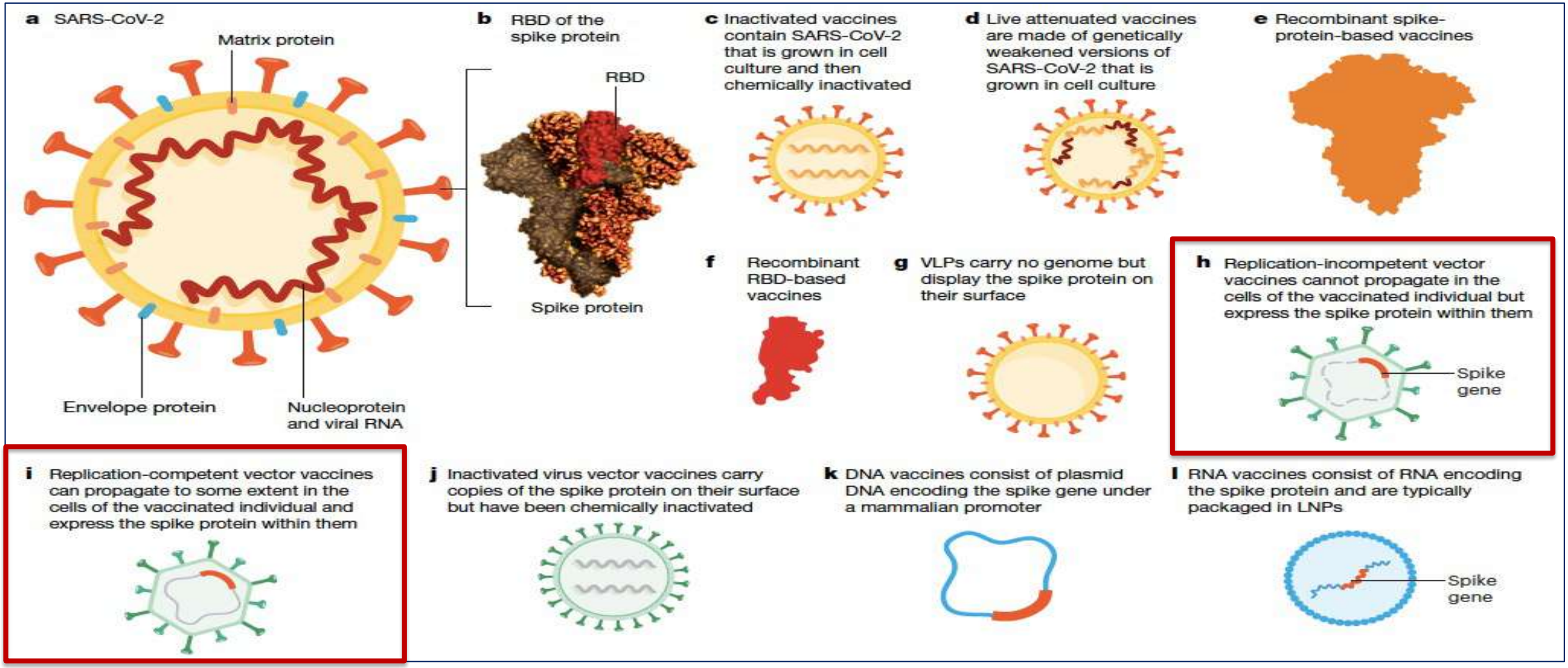
Table 5. Status of chimpanzee adenovirus vector (ChAd) vaccine development for a range of outbreak pathogens at the Jenner Institute, University of Oxford (as May 2017). The genetic background for all vectors is ChAdOx1 (a species E modified chimpanzee adenovirus based on isolate Y25).[23] Antigens are inserted at the E1 locus via Gateway® recombination. For preclinical immunogenicity testing, mice typically receive a single-dose of 10^8 infectious units (intramuscular).

Pathogen	ChAd construct made	Immunogenicity demonstrated in mice	Neutralising antibody activity demonstrated	Animal efficacy demonstrated	GMP production funded	Phase I/II evaluation commenced
Pandemic Influenza virus	✓	✓	✓	✓	✓	✓
Rift Valley Fever virus	✓	✓	✓	✓	✓	
MERS CoV	✓	✓	✓	✓	✓	
Zika virus	✓	✓		✓	✓	
Chikungunya virus	✓	✓	✓		✓	
Crimean Congo Haemorrhagic Fever virus	✓	✓				
Lassa virus	✓	✓				
Zaire ebolavirus	✓	✓				
Sudan ebolavirus	✓	✓				
Zaire + *Sudan ebolavirus* + Marburg	✓	✓				
Yersinia pestis	✓	✓				
Nipah virus	✓	✓				
SARS CoV	✓	✓				

Ewer et al. Human Vaccines Immunotherapeutics 2017

SALGIN AŞILAMASINDA ADENOVİRÜS VEKTÖRLERİ

COVID-19 AŞILARI

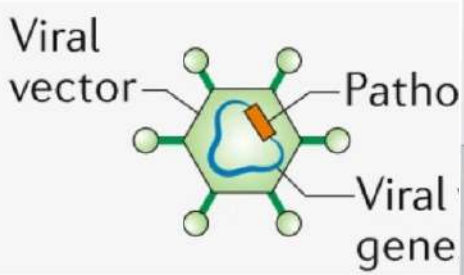


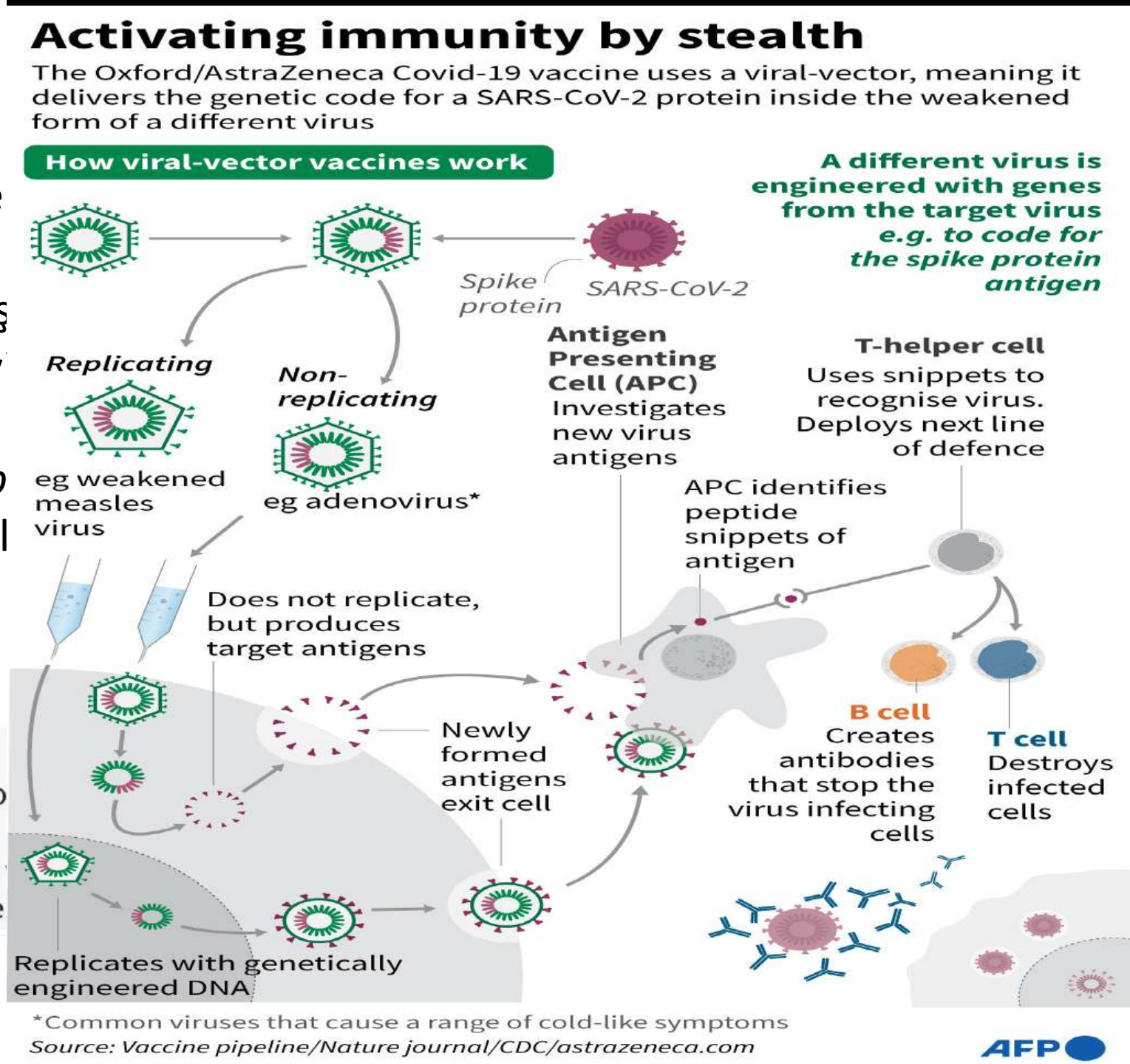
Florian Kramer. Nature 2020

VİRAL VEKTÖR AŞILARI

- **Viral Vektör**: korunmanın hedefle
  dağıtımının sağlanması
  - Viral vektör kendisi hastalık oluş
  - Vektör olarak en sık kullanılan v

  - Hücre içinde çoğalabilenler (*rep*
  - Anahtar genler devre dışı bırakıl





VİRAL VEKTÖR AŞILARI

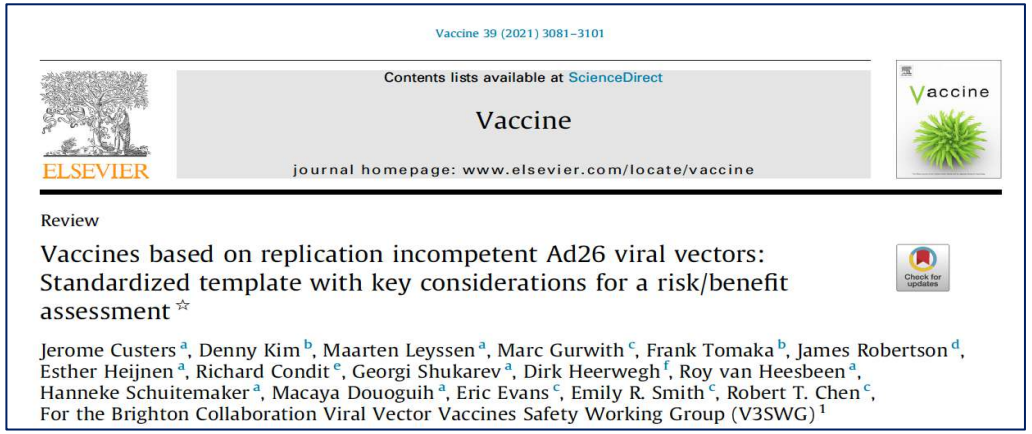
- **Viral Vektör**: korunmanın hedeflendiği enfeksiyon hastalığına ait antijenleri taşıyan ve dağıtımının sağlanması
  - Viral vektör kendisi hastalık oluşturmayacak şekilde programlanmıştır.
  - Vektör olarak en sık kullanılan virüsler: Adenovirüs, Kızamık, Vaccinia virüs

- Viral vektörler
  - Hücre içinde çoğalabilenler (*replicating*)
  - Anahtar genler devre dışı bırakıldığı için çoğalma yeteneği olmayanlar (*non-replicating*)

- COVID-19 aşısı öncesi EBOLA aşısında (vektörü veziküler stomatir virüsü) çalışmaları yapılmış ve onay almıştır.
- Viral vektör aşılarının dezavantajı, insanlar daha önce viral vektöre maruz kalmışsa ve buna karşı bir bağışıklık tepkisi geliştirmişse, potansiyel olarak aşının etkinliğini azaltabilmesidir.

VİRAL VEKTÖR AŞILARI

5.19. What is known about the effect of pre-existing immunity, including both natural immunity and repeat administration of the vector or the vaccine, on 'take', safety or efficacy in any animal model or human studies using this vector?



Vaccine 39 (2021) 3081–3101

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Vaccines based on replication incompetent Ad26 viral vectors: Standardized template with key considerations for a risk/benefit assessment ☆

Jerome Custers [a], Denny Kim [b], Maarten Leyssen [a], Marc Gurwith [c], Frank Tomaka [b], James Robertson [d], Esther Heijnen [a], Richard Condit [e], Georgi Shukarev [a], Dirk Heerwegh [f], Roy van Heesbeen [a], Hanneke Schuitemaker [a], Macaya Douoguih [a], Eric Evans [c], Emily R. Smith [c], Robert T. Chen [c], For the Brighton Collaboration Viral Vector Vaccines Safety Working Group (V3SWG) [1]

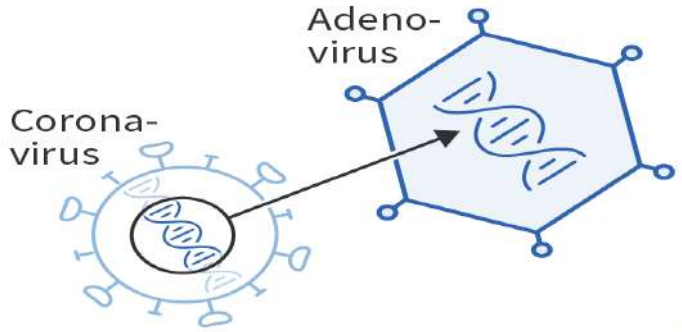
Data acquired to date, in more than 6,000 vaccinated human participants, have not revealed impact of pre-existing vector immunity on the vaccine insert specific humoral or cellular response. Repeated administration with the Ad26 vector leads to an increase in antigen specific humoral responses and a maintenance of cellular responses. With more than 114,000 participants vaccinated overall, no safety issues have been identified.

Custers et al. Vaccine 2021

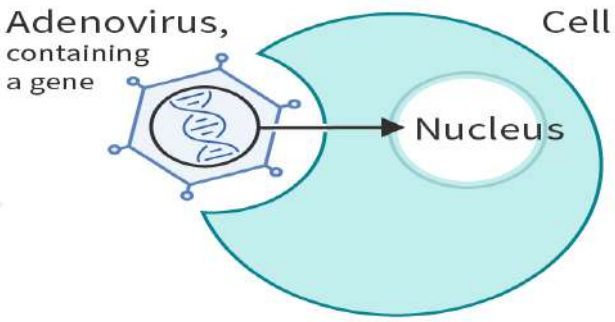
VİRAL VEKTÖR AŞILARI

How does the vector vaccine work against coronavirus?

thl

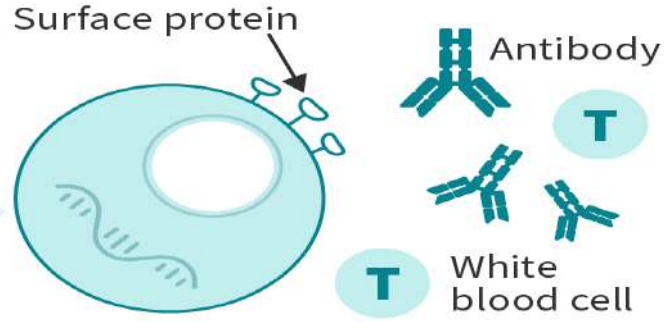


A coronavirus contains a gene that directs cells to produce the coronavirus surface protein (spike protein). In the vaccine, this gene has been turned into a part of the genome of a harmless carrier virus.



The carrier virus takes the gene into a cell at the injection site.

The carrier virus for the corona-virus vaccine is an adenovirus. It cannot reproduce inside the body.



The cell starts producing surface protein on its surface according to the instruction of the gene. The body recognises the protein doesn't belong there and starts to fight it off.

#coronavirus

Illustration.
Sources: Nature, THL 2020

VİRAL VEKTÖR AŞILARI

Seminars in Immunology 50 (2020) 101430

Contents lists available at ScienceDirect

Seminars in Immunology

journal homepage: www.elsevier.com/locate/ysmim

Review

New viral vectors for infectious diseases and cancer

Emanuele Sasso [a,b,1], Anna Morena D'Alise [a,1], Nicola Zambrano [b,c], Elisa Scarselli [a], Antonella Folgori [d], Alfredo Nicosia [b,c,*]

Sasso et al. Seminars in Immunology 2020

VİRAL VEKTÖR AŞILARI

Since the discovery in 1796 by Edward Jenner of vaccinia virus as a way to prevent and finally eradicate smallpox, the concept of using a virus to fight another virus has evolved into the current approaches of viral vectored genetic vaccines. In recent years, key improvements to the vaccinia virus leading to a safer version (Modified Vaccinia Ankara, MVA) and the discovery that some viruses can be used as carriers of heterologous genes encoding for pathological antigens of other infectious agents (the concept of 'viral vectors') has spurred a new wave of clinical research potentially providing for a solution for the long sought after vaccines against major diseases such as HIV, TB, RSV and Malaria, or emerging infectious diseases including those caused by filoviruses and coronaviruses. The unique ability of some of these viral vectors to stimulate the cellular arm of the immune response and, most importantly, T lymphocytes with cell killing activity, has also reawakened the interest toward developing therapeutic vaccines against chronic infectious diseases and cancer. To this end, existing vectors such as those based on Adenoviruses have been improved in immunogenicity and efficacy. Along the same line, new vectors that exploit viruses such as Vesicular Stomatitis Virus (VSV), Measles Virus (MV), Lymphocytic choriomeningitis virus (LCMV), cytomegalovirus (CMV), and Herpes Simplex Virus (HSV), have emerged. Furthermore, technological progress toward modifying their genome to render some of these vectors incompetent for replication has increased confidence toward their use in infant and elderly populations. Lastly, their production process being the same for every product has made viral vectored vaccines the technology of choice for rapid development of vaccines against emerging diseases and for 'personalised' cancer vaccines where there is an absolute need to reduce time to the patient from months to weeks or days.

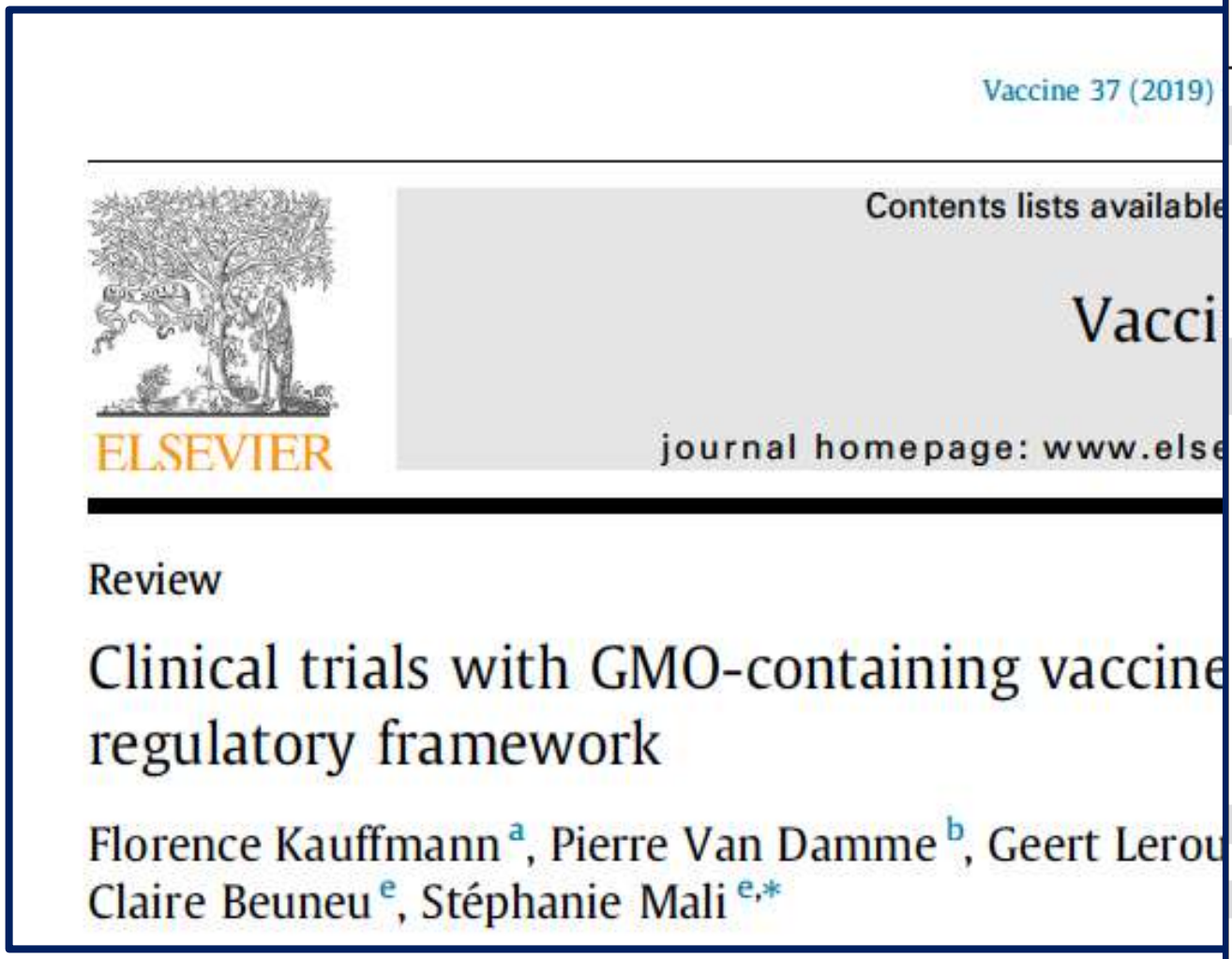
Here we review the recent developments in viral vector technologies, focusing on novel vectors based on primate derived Adenoviruses and Poxviruses, Rhabdoviruses, Paramixoviruses, Arenaviruses and Herpesviruses. We describe the rationale for, immunologic mechanisms involved in, and design of viral vectored gene vaccines under development and discuss the potential utility of these novel genetic vaccine approaches in eliciting protection against infectious diseases and cancer.

ener çağrı dinleyici

Sasso et al. Seminars in Immunology 2020

VİRAL VEKTÖR AŞILARI

REGÜLASYON



Vaccine 37 (2019)

Contents lists available

Vacci

journal homepage: www.else

ELSEVIER

Review

Clinical trials with GMO-containing vaccine regulatory framework

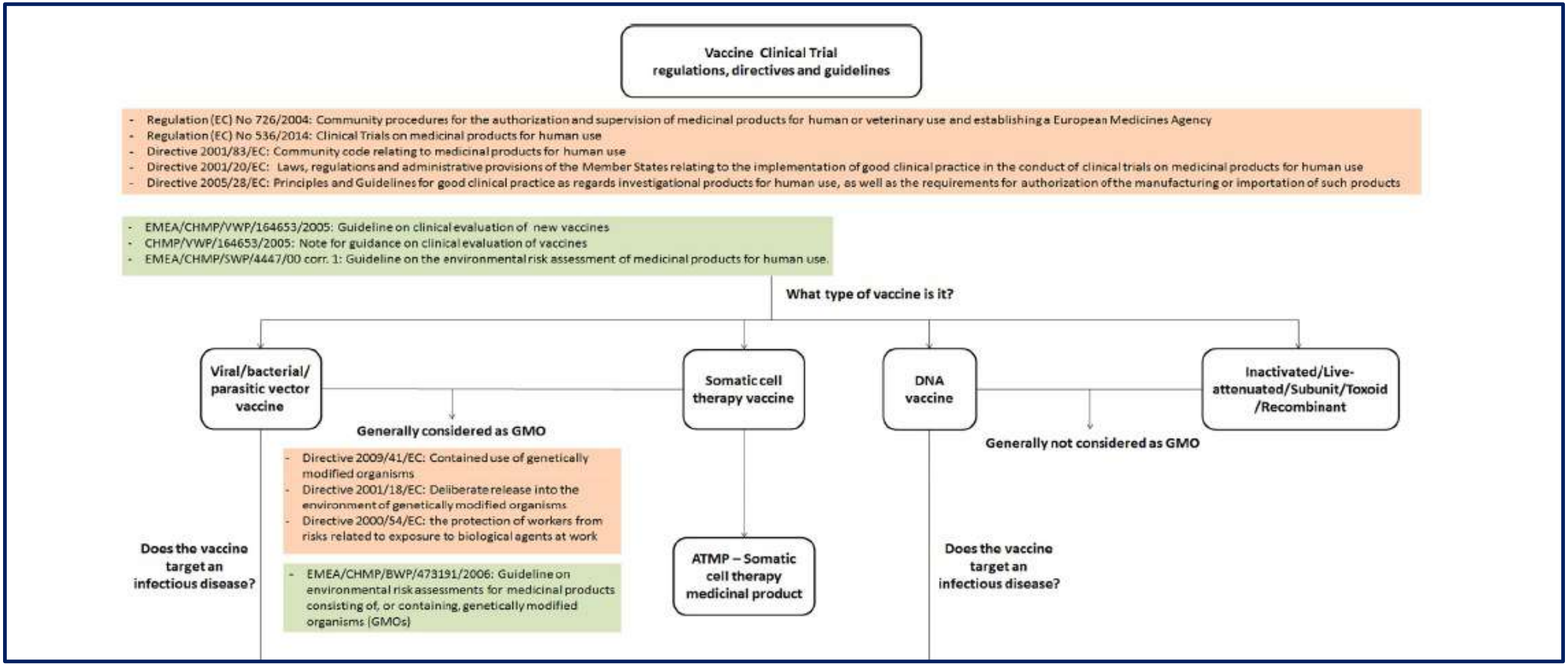
Florence Kauffmann [a], Pierre Van Damme [b], Geert Lerou
Claire Beuneu [e], Stéphanie Mali [e,*]

Number° of GMO-containing vaccine clinical trials per country in Europe: 2004-2017	Absolute n°	% (out of 147 trials)
Austria	4	2.7
Belgium	13	8.8
Bulgaria	2	1.4
Czech republic	2	1.4
Denmark	3	2.0
Estonia	1	0.7
Finland	5	3.4
France	14	9.5
Germany	18	12.2
Hungary	7	4.8
Iceland	1	0.7
Ireland	1	0.7
Italy	4	2.7
Lithuania	1	0.7
Netherlands	8	5.4
Norway	1	0.7
Poland	3	2.0
Romania	1	0.7
Slovakia	1	0.7
Spain	16	10.9
Sweden	4	2.7
UK	91	61.9
TOTAL including all multi-country trials	201	NA
TOTAL representing each multi-country trial as one trial	147	100

Kauffman et al. Vaccine 2021

VİRAL VEKTÖR AŞILARI

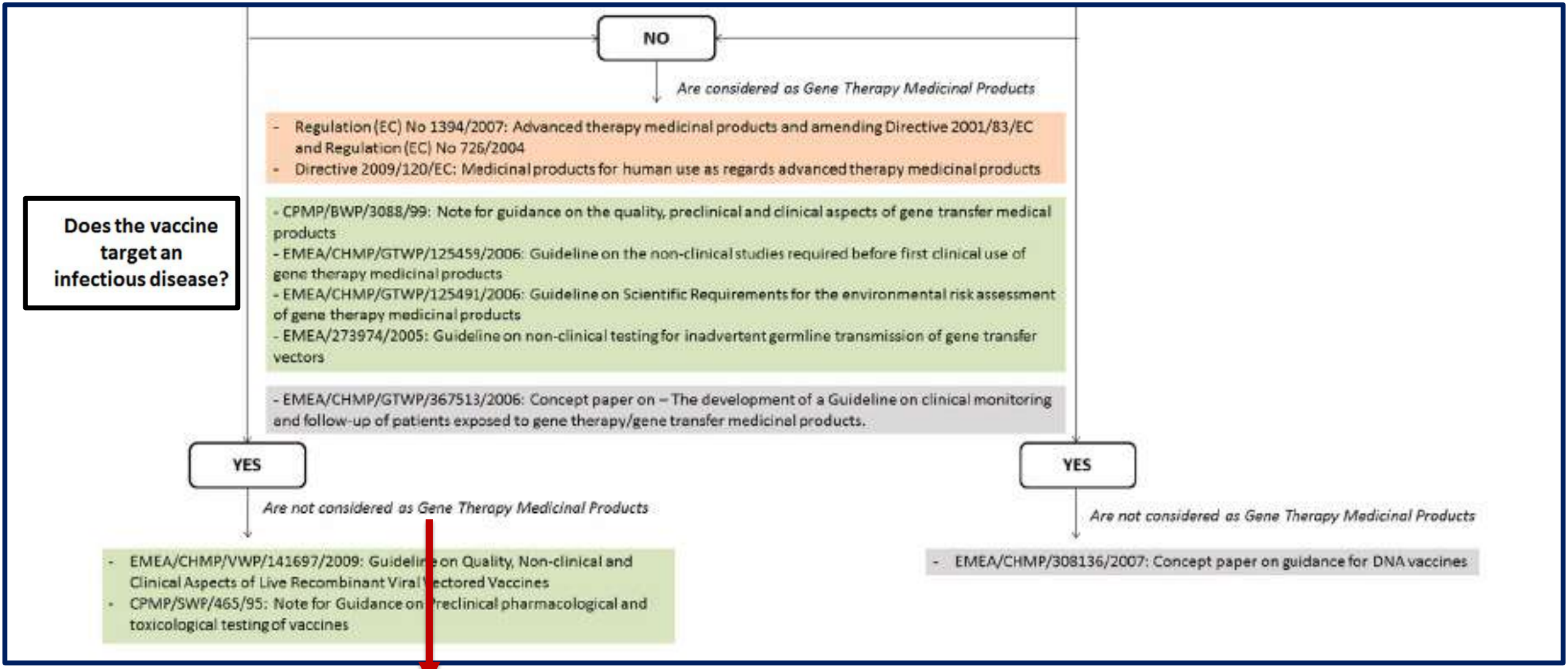
REGÜLASYON



Kauffman et al. Vaccine 2021

VİRAL VEKTÖR AŞILARI

REGÜLASYON



Enfeksiyon hastalıklarına yönelik olarak geliştirilen aşılar, Gen Tedavisi olarak kabul edilmemektedir.

Kauffman et al. Vaccine 2021

VİRAL VEKTÖR AŞILARI

REGÜLASYON

Vaccine 39 (2021) 3067–3080

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/vaccine

Review

The Brighton Collaboration standardized template for collection of key information for risk/benefit assessment of a Modified Vaccinia Ankara (MVA) vaccine platform

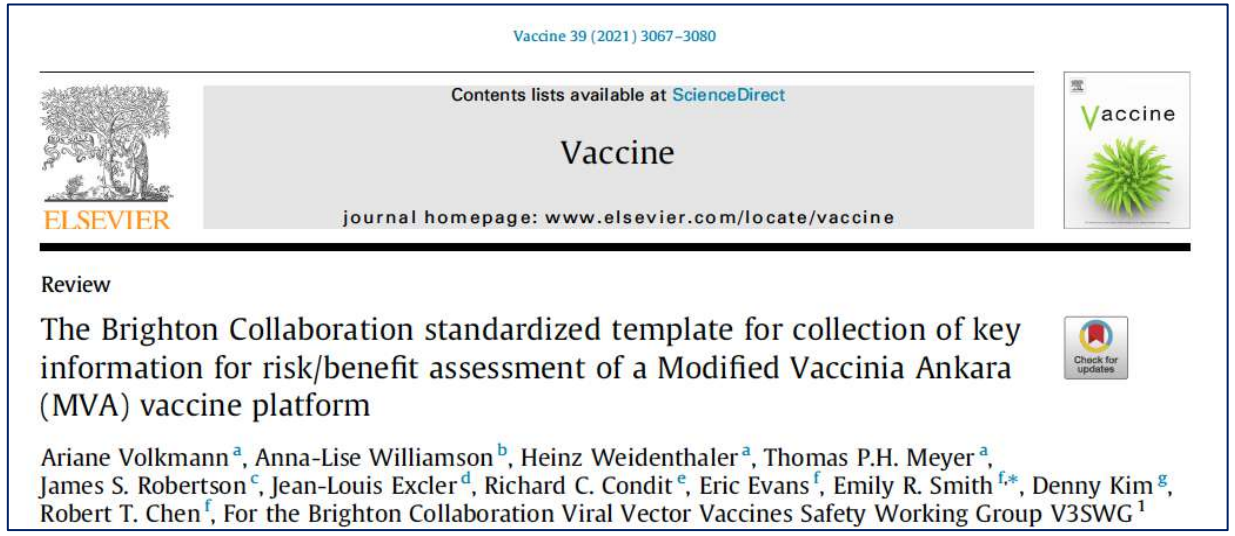
Ariane Volkmann [a], Anna-Lise Williamson [b], Heinz Weidenthaler [a], Thomas P.H. Meyer [a], James S. Robertson [c], Jean-Louis Excler [d], Richard C. Condit [e], Eric Evans [f], Emily R. Smith [f,*], Denny Kim [g], Robert T. Chen [f], For the Brighton Collaboration Viral Vector Vaccines Safety Working Group V3SWG [1]

Volkman et al. Vaccine 2021

VİRAL VEKTÖR AŞILARI

REGÜLASYON

3.6. What is the risk of integration into the human genome?



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Very low

Poxviral vectors are considered non-integrating according to the EMA '*Guideline on nonclinical testing for inadvertent germline transmission of gene transfer vectors*', because they lack the machinery to actively integrate their genome into the host chromosomes.[1] MVA, as well as other members of the Poxviridae family, is unusual among deoxyribonucleic acid (DNA) viruses in that they replicate in the cytoplasmic compartment of the cell. Compared to other DNA viruses, the possibility for integration of their genetic material into the host chromosome is therefore extremely low [47].
In addition, vaccinia infection results in cell death

Volkman et al. Vaccine 2021

VİRAL VEKTÖR AŞILARI

REGÜLASYON

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VİRAL VEKTÖR AŞILARI

REGÜLASYON

3.6. What is the risk of integration into the human genome? Negligible

Vaccine 39 (2021) 3081–3101

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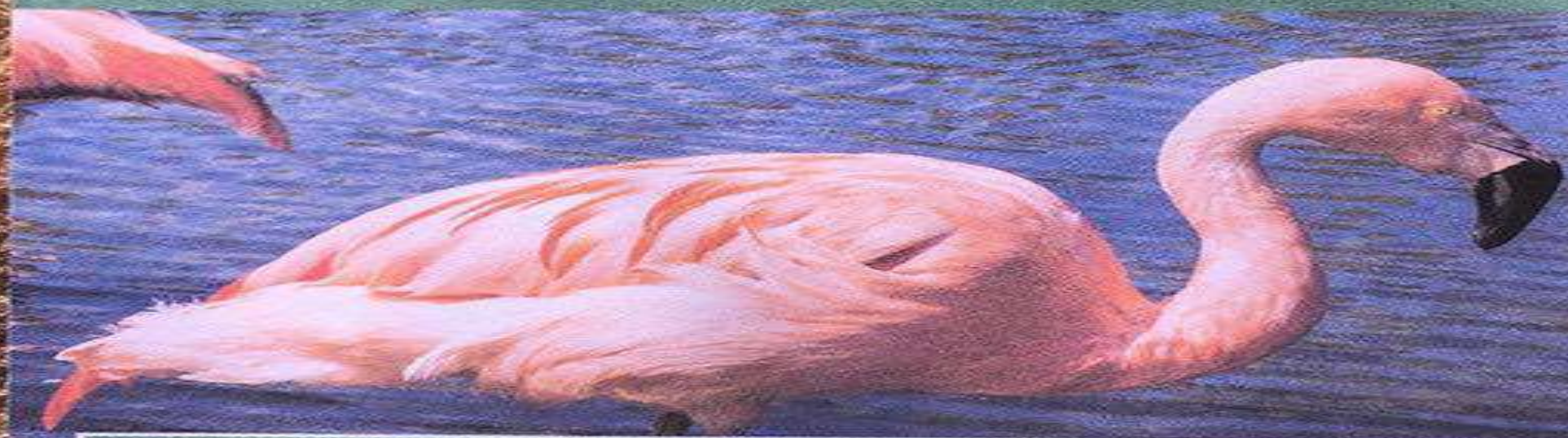
Adenoviruses are considered non-integrating according to the EMA 'Guideline on nonclinical testing for inadvertent germline transmission of gene transfer vectors', because they lack the machinery to actively integrate their genome into the host chromosomes. The adenoviral genome remains epichromosomal, thus avoiding the risk of integration of the viral DNA into the host genome following cell infection. Therefore, chromosomal integration of genetic material of Ad26 in the human host is unlikely.

Custers et al. Vaccine 2021

ANIMAL FACT



Flamingos are monogamous. Except for Phillip, that cheating bastard.

Los Angeles Zoo obvious plant

VİRAL VEKTÖR AŞILARI

VİRAL HEMORAJİK ATEŞ

Viral hemorrhagic fevers

Order	Fa
Amarillovirales	Fl
Bunyavirales	Ar
	Ha
	Na
	Ph
Mononegavirales	Fil

Vaccinia virus strains used for smallpox vaccines.

Virus strain	Parental strain	Vaccine generation [a]	LD_{50} (pfu) [b]
Ikeda		First	≤6.3x10^5
NYCBH		First	2.9x10^6
CV1-78		First	≤6.3x10^5
Lister (Elstree)		First	6.3x10^6
EM63	NYCBH	First	1.4x10^7
Dairen-I		First	
ACAM1000	NYCBH	Second	
ACAM2000	ACAM1000	Second	
LC16	Lister	Third	≥6.3x10^8
DIs	Dairen-I	Third	≥6.3x10^8
MVA	Ankara	Third	
LC16m8	LC16	Third	
LC16m8Δ	Lc16m8	Fourth	
NYVAC	Copenhagen	Fourth	
MVTT	Tian Tan	Fourth	
E3L deletion mutants		Fourth	

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uth Korea, Vietnam,

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Yoshikova et al. Vaccine 2021

VİRAL VEKTÖR AŞILARI

EBOLA AŞILARI

International Journal of Infectious Diseases 74 (2

Contents lists available at ScienceDire

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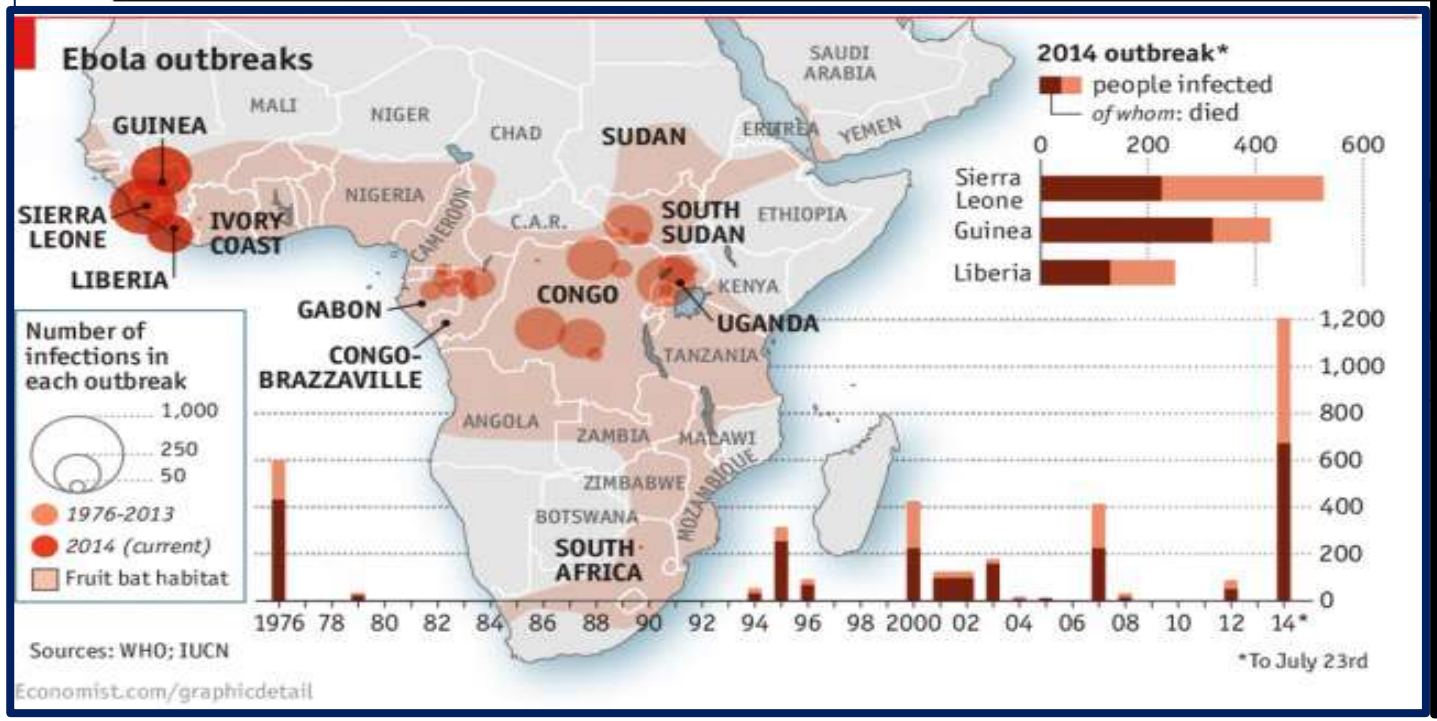
International Journal of Infectiou

journal homepage: www.elsevier.com/l



Vaccine platform
DNA vaccine (plasmid)
Adenovirus 26
Adenovirus 26 then adenovirus 35
Adenovirus 35
Adenovirus 5
DNA vaccine (plasmid)/adenovirus 5
CAdVax
Chimpanzee adenovirus 3
Chimpanzee adenovirus 63
HPIV3
MVA
NDV
RhCMV
Whole-virus vaccine
VLP
VLP Kunjin
VRP VEEV
VSV

ener çağrı dinleyici

VİRAL VEKTÖR AŞILARI

EBOLA AŞILARI

Table 2

Status of candidate Ebola vaccines

Company/institution/ country	(Vaccine name)/Ebola component glycoprotein	Vector	Administration	Storage temperature	Target population	Comments
Merck USA/Public Health Agency Canada	(Ervebo)Recombinant VSV-ZEBOV-Ebola Kikwit strain Replication competent vaccine	VSV	Single dose	60°C to −80°C for 36 months and 2°C–8°C for 14 says	Active immunization (reactive use) of at risk subjects ≥18 years of age	2016- granted Breakthrough Therapy Designation by the US FDA and PRIME status by the European Medicines Agency (EMA) and in 2019, granted medical use in EU and USA. Used extensively in the Kivu Ebola epidemic under a compassionate use protocol
Johnson & Johnson (USA) and MVA-BN Filo, Bavarian Nordic (Denmark)	(Zabdeno)MVA-BN-Filo encodes Ebola virus, Sudan virus, and Marburg virus glycoproteins, and Tai Forest virus nucleoprotein	Human adenoviral serotype 26 or MVA	Heterologous prime boost regimen	Ad26.ZEBOV: 20°C or 60°C for up to 60 months and +2 to +8°C for up to 12 months MVA-BN-Filo: 20°C or 60°C for up to 60 months and +2 to +8°C for up to 6 months	Adults and children ≥ 1 year of age	Granted approval by Committee for Medial Products for Human Use -European Medicines Agency (CHMP-EMA) in 2020 as a two-dose regimen for the prevention of Ebola virus disease. Seeking licensure under the Animal Rule and/or to European Medicines Agency. Collaborative.
GlaxoSmithKline (UK) and, for MVA-BN-Filo, Bavarian Nordic (Denmark)- NIAID/GSK	(ChAd3-EBO-Z) with or without MVA-BN-Filo Ebola virus, Mayinga strain (1976)	Chimpanzee adenoviral serotype 3 or MVA	Single dose or heterologous prime-boost regimen			**Ongoing clinical evaluationl**
Academy of Military Medical Sciences and CanSino Biologics (China)	(Ad5-ZEBOV) Ebola virus, Makona strain (2014)	Human Adenoviral serotype 5	Single dose or homologous prime-boost regimen	Freeze-dried powder, stable for more than 2 weeks even if kept at a temperature of 37°C;		Licensed in China

ener çağrı dinleyici

VİRAL VEKTÖR AŞILARI

EBOLA AŞILARI

Gamalei Scientific Research Institute of Epidemiology and Microbiology (Russia)	(GamEvac-Combi and GamEvac-Lyo) Monovalent Zaire (Makona)	VSV and Ad5-vectored vaccine	Heterologous prime boost regimen	16°C to −20°C for 12 months 4°C for lyophilized formulation	18–55 years	Licensed in Russia
Novavax, USA	(NVX-CoV2373). Nanoparticle recombinant Ebola GP Vaccine) Monovalent Zaire (Makona)	Contains the full-length SARS-CoV-2 spike protein and Novavax' patented Matrix-M1 adjuvant	2 doses 21 days apart,	2° to 8°C for six months, and 24 hours at room temperature	18–65 years	Efficacy 89.3 %.
Inovio Pharmaceuticals, USA	(INO-4201 DNA vaccine) Plasmid of Ebola outbreak strains from 1976–2006		2 doses four weeks apart	+2°C to +8°C for 3 years and 25°C for 1 year 37°C for 1 month 60°C for several days	≥ 18 years	In 95% (170/179) of evaluable subjects generated an Ebola-specific antibody immune response,
FBRI SRC VB VECTOR, Rospotrebnadzor, Russia	(EpivacEbola) Monovalent Zaire (Makona)		2 doses (prime + boost on 28 days)	2–8°C for 1 year Can extend shelf life to 2 years	18–55 years	Licensed in Russia since 2016

VİRAL VEKTÖR AŞILARI

EBOLA AŞILARI

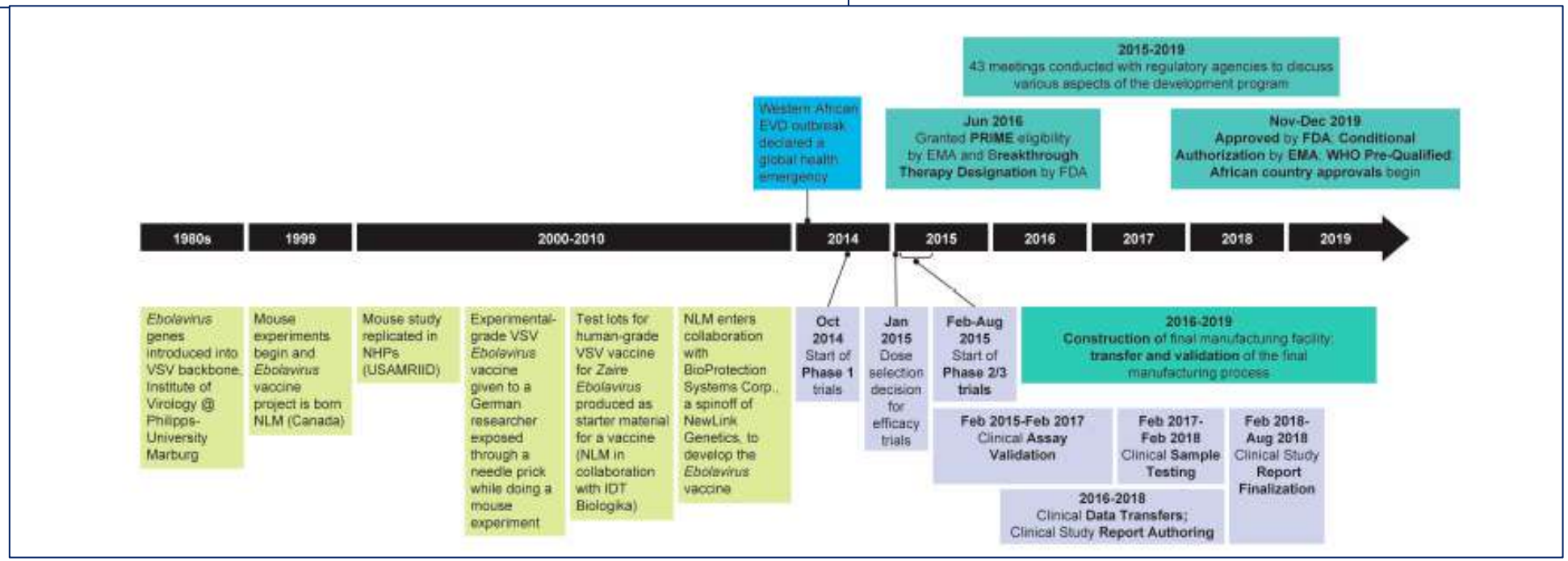
vaccines

MDPI

Review

Development of Pandemic Vaccines: ERVEBO Case Study

Jayanthi Wolf [1], Risat Jannat [2], Sheri Dubey [3], Sean Troth [4], Matthew T. Onorato [5], Beth-Ann Coller [6], Mary E. Hanson [7] and Jakub K. Simon [6,*]

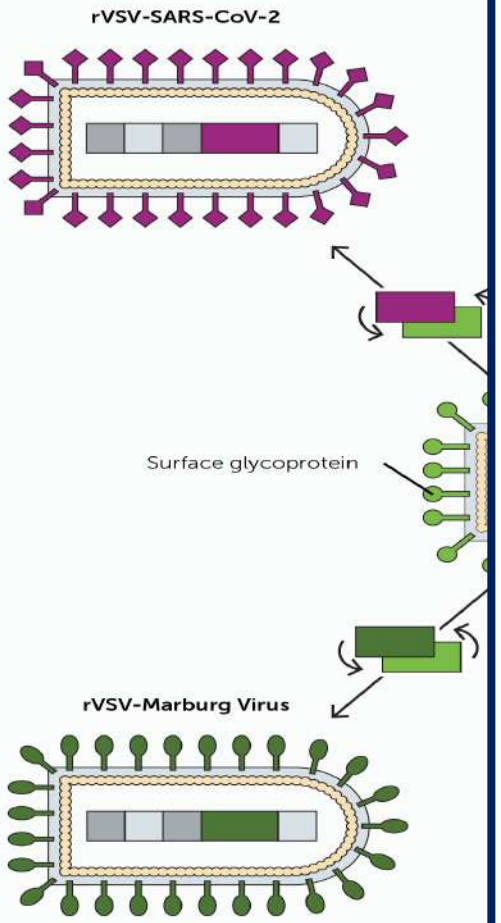


ener çağrı dinleyici

VİRAL VEKTÖR AŞILARI

IAVI's VSV EID vaccine platform

1. When VSV infects its natural host, a strong immune response develops against the surface glycoprotein.
2. VSV is recombimantly modified (rVSV) by replacing the gene that codes for its surface glycoprotein with a gene coding for the surface glycoprotein from a target virus.
3. When given as a vaccine, rVSV infects cells in the body and produces new virus coated with the surface glycoprotein from the target virus.
4. The immune system responds by producing antibodies against the surface glycoprotein from the target virus.
5. If the vaccinated person later encounters the target virus, memory cells from the immune system rapidly produce antibodies that block the infection and prevent disease.



EIDs by the numbers

50%
average case fatality rate for Ebola virus and Marburg virus disease

100,000–300,000
cases of Lassa fever occur annually

15%
average case fatality rate for people hospitalized with Lassa fever

> 263 million
confirmed cases of COVID-19 in 23 months

100%
efficacy for the rVSV-vectored Ebola Zaire vaccine in a Phase III trial

3
IAVI EID vaccines in preclinical development; 1 in clinical development

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COVID19 AŞILARI

World Health Organization

R&DBlueprint
Powering research to prevent epidemics

COVID-19 - Landscape of novel coronavirus candidate vaccine development worldwide

11 Şubat 2022 Cuma

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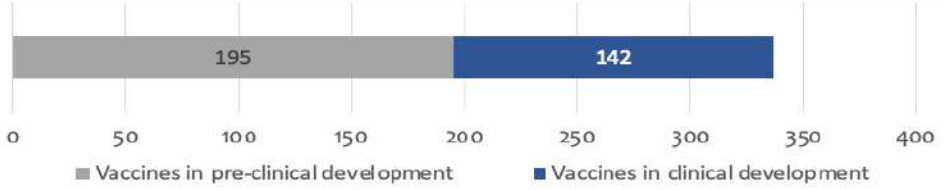
Summary Information on Vaccine Products in Clinical Development

1. - Number of vaccines in clinical development 142

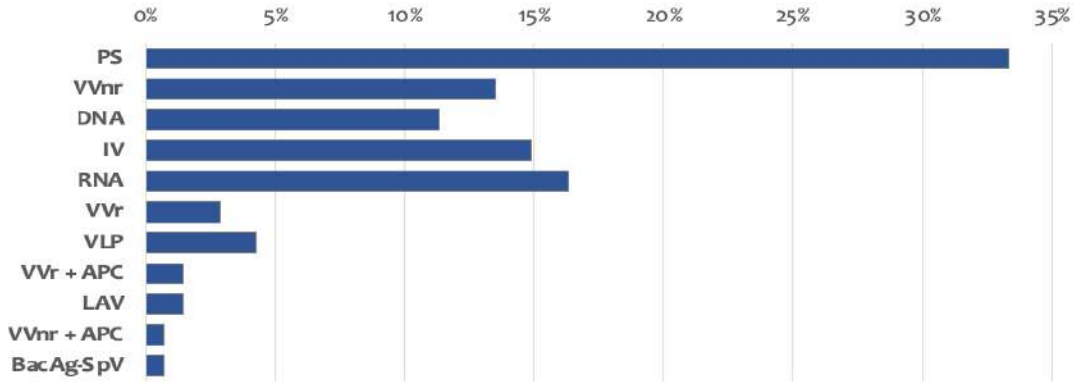
2. - Number of vaccines in pre-clinical development 195



3. - Candidates in clinical phase

Filter: All — Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	47	33%
VVnr	Viral Vector (non-replicating)	19	13%
DNA	DNA	16	11%
IV	Inactivated Virus	21	15%
RNA	RNA	22	16%
VVr	Viral Vector (replicating)	4	3%
VLP	Virus Like Particle	6	4%
VVr + APC	VVr + Antigen Presenting Cell	2	1%
LAV	Live Attenuated Virus	2	1%
VVnr + APC	VVnr + Antigen Presenting Cell	1	1%
BacAg-SpV	Bacterial antigen-spore expression vector	1	1%
		142	



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4	VVnr	Viral vector (Non-replicating)	ChAdOx1-S - (AZD1222)	1-2	Day 0 + 28	IM	AstraZeneca + University of Oxford	Phase 4
5	VVnr	Viral vector (Non-replicating)	Recombinant novel coronavirus vaccine (Adenovirus type 5 vector)	1	Day 0	IM	CanSino Biological Inc./Beijing Institute of Biotechnology	Phase 4
6	VVnr	Viral vector (Non-replicating)	Recombinant COVID-19 vaccine (adenovirus type 5 vector) for Inhalation (Ad5-nCoV-IH)	1	Day 0	IH	CanSino Biological Inc./Beijing Institute of Biotechnology	Phase 3
7	VVnr	Viral vector (Non-replicating)	Gam-COVID-Vac Adeno-based (rAd26-S+rAd5-S)	2	Day 0 + 21	IM	Gamaleya Research Institute ; Health Ministry of the Russian Federation	Phase 3
8	VVnr	Viral vector (Non-replicating)	Ad26.COV2.S	1-2	Day 0 or Day 0 +56	IM	Janssen Pharmaceutical	Phase 4
26	VVnr	Viral vector (Non-replicating)	GRAd-COV2 (Replication defective Simian Adenovirus (GRAd) encoding S)	1	Day 0	IM	ReiThera + Leukocare + Univercells	Phase 2/3
27	VVnr	Viral vector (Non-replicating)	VXA-CoV2-1 Ad5 adjuvanted Oral Vaccine platform	2	Day 0 + 28	Oral	Vaxart	Phase 2
28	VVnr	Viral vector (Non-replicating)	MVA-SARS-2-S	2	Day 0 + 28	IM	University of Munich (Ludwig-Maximilians)	Phase 1
		Viral vector (Replicating)	V591-001 - Measles-vector based (TMV-o38)	1-2	Day 0 + 28	IM	Merck & Co. + Themis + Sharp & Dohme + Institute Pasteur	Phase 1/2
38	VVr	Viral vector (Replicating)	DelNS1-2019-nCoV-RBD-OPT1 (Intranasal flu-based-RBD)	2	Day 0 + 28	IN	University of Hong Kong, Xiamen University and Beijing Wantai Biological Pharmacy	Phase 3
42	VVr + APC	Viral vector (Replicating) + APC	Covid-19/aAPC vaccine. The Covid-19/aAPC vaccine is prepared by applying lentivirus modification with immune modulatory genes and the viral minigenes to the artificial antigen presenting cells	3	Day 0 + 14 + 28	SC	Shenzhen Geno-Immune Medical Institute	Phase 1
43	VVnr + APC	Viral vector (Non-replicating) + APC	LV-SMENP-DC vaccine. Dendritic cells are modified with lentivirus vectors expressing Covid-19 minigene SMENP and immune modulatory genes. CTLs are activated by LV-DC presenting Covid-19	1	Day 0	SC & IV	Shenzhen Geno-Immune Medical Institute	Phase 1/2
49	VVnr	Viral vector (Non-replicating)	Human Adenovirus Type 5: hAd5 S+N bivalent vaccine (S-Fusion + N-ETSD). E2b- Deleted Adeno.	1-2	Day 0 + 21	SC or Oral or SL	ImmunityBio, Inc	Phase 1/2
50	VVnr	Viral vector (Non-replicating)	COH04S1 (MVA-SARS-2-S) - Modified vaccinia ankara (sMVA) platform + synthetic SARS-CoV-2	1-2	Day 0 + 28	IM	City of Hope Medical Center + National Cancer Institute	Phase 1
51	VVr	Viral vector (Replicating)	rVSV-SARS-CoV-2-S Vaccine (IIBR-100)	1	Day 0	IM	Israel Institute for Biological Research	Phase 2/3
52	VVr + APC	Viral vector (Replicating) + APC	Dendritic cell vaccine AV-COVID-19. A vaccine consisting of autologous dendritic cells loaded	1	Day 0	IM	Aivita Biomedical, Inc;	Phase 2
58	VVnr	Viral vector (Non-replicating)	AdCLD-CoV19 (adenovirus vector)	1	Day 0	IM	Cellid Co., Ltd.	Phase 1/2
		Viral vector (Non-replicating)	AdCOVID, Adenovirus-based platform expresses receptor-binding domain (RBD) of spike protein	1-2	Day 0	IN	Altimmune, Inc.	Phase 1
71	VVnr	Viral vector (Non-replicating)	BBV154, Adenoviral vector COVID-19 vaccine	1	Day 0	IN	Bharat Biotech International Limited	Phase 1
77	VVnr	Viral vector (Non-replicating)	Chimpanzee Adenovirus serotype 68 (ChAd) and self-amplifying mRNA (SAM) vectors expressing spike alone, or spike plus additional SARS-CoV-2 T cell epitopes.	2-3	Day 0 + 14 + 28 or Day 0 +28 + 56 or Day 0 + 112	IM	Gritstone Oncology	Phase 1
88	VVr	Viral vector (Replicating)	COVIVAC. Newcastle Disease Virus (NDV) expressing membrane-anchored pre-fusion-stabilized trimeric SARS-CoV-2 S protein +/- adjuvant CpG 1018	2	Day 0 + 28	IM	Institute of Vaccines and Medical Biologicals, Vietnam	Phase 1/2
89	VVnr	Viral vector (Non-replicating)	SC-Ad6-1, Adneviral vector vaccine	1-2	Day 0 +/- 21	IM	Tetherex Pharmaceuticals Corporation	Phase 2
101	VVnr	Viral vector (Non-replicating)	Modified Vaccinia Virus Ankara (MVA) vector expressing a stabilized SARS-CoV-2 spike protein	2	Day 0 + 28	IM	German Center for Infection Research	Phase 1/2
109	VVnr	Viral vector (Non-replicating)	PIV5 vector that encodes the SARS-CoV-2 spike protein	1	Day 0	IN	CyanVac LLC	Phase 1
110	VVnr	Viral vector (Non-replicating)	AZD2816; adenoviral vector ChAdOx platform and based on the Beta (B.1.351) variant	2	Day 0 + 28	IM	AstraZeneca + University of Oxford	Phase 2/3
121	VVnr	Viral vector (Non-replicating)	AAV5-RBD-S vaccine (BCD-250), A recombinant Adenovirus-Associated viral Vector (AAV-5) encoding spike protein	1	Day 0	IM	Biocad	Phase 1/2
131	VVnr	Viral vector (Non-replicating)	Ad5-triCoV/Mac or ChAd-triCoV/Mac, new experimental adenovirus-based vaccines expressing SARS-CoV-2 spike, nucleocapsid and RNA polymerase proteins	1	Day 0	AE	McMaster University	Phase 1
140	VVr	Viral vector (Replicating)	NDV-HXP-S; A Live Recombinant Newcastle Disease Virus-vectored COVID-19 Vaccine	1	Day 0	IN/IM	Sean Liu, Icahn School of Medicine at Mount Sinai	Phase 1

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32	VVnr	Viral vector (Non-replicating)	Sendai virus vector	SARS-CoV2		ID Pharma
33	VVnr	Viral vector (Non-replicating)	Sendai virus vector	[illegible]	[illegible]	[illegible]
34	VVnr	Viral vector (Non-replicating)	Adenovirus-based	SARS-CoV2		Ankara University
35	VVnr	Viral vector (Non-replicating)	Adeno-associated virus vector (AAVCOVID)	[illegible]		[illegible]
36	VVnr	Viral vector (Non-replicating)	MVA encoded VLP	SARS-CoV2	LASV, EBOV, MARV, HIV	GeoVax/BravoVax
37	VVnr	Viral vector (Non-replicating)	MVA-S	SARS-CoV2		IDIBAPS-Hospital Clinic, Spain
38	VVnr	Viral vector (Non-replicating)	Adeno5-based	SARS-CoV2		Erciyes University
39	VVnr	Viral vector (Non-replicating)	Ad5 S (GREVAX™ platform)	SARS-CoV2	MERS	Greffex
40	VVnr	Viral vector (Non-replicating)	Oral Ad5 S	SARS-CoV2	Zika, VZV, HSV-2 and Norovirus	Stabilitech Biopharma Ltd
41	VVnr	Viral vector (Non-replicating)	Adenovirus-based + HLA-matched peptides	Pan-Corona		Valo Therapeutics Ltd
42	VVnr	Viral vector (Non-replicating)	MVA expressing structural proteins	SARS-CoV2	Multiple candidates	Centro Nacional Biotecnología (CNB-CSIC), Spain
43	VVnr	Viral vector (Non-replicating)	Parainfluenza virus 5 (PIV5)-based vaccine expressing the spike protein	SARS-CoV2	MERS	University of Georgia/University of Iowa
44	VVnr	Viral vector (Non-replicating)	Recombinant deactivated rabies virus containing S1	SARS-CoV2	HeV, NiV, EBOV, LASSA, CCHFV, MERS	Bharat Biotech/Thomas Jefferson University
45	VVnr	Viral vector (Non-replicating)	Influenza A H1N1 vector	SARS-CoV2		National Research Centre, Egypt
46	VVnr	Viral vector (Replicating)	Newcastle disease virus expressing the spike protein	SARS-CoV2		Icahn School of Medicine at Mount Sinai
47	VVnr	Viral vector (Non-replicating)	Newcastle disease virus expressing membrane-anchored spike	SARS-CoV2		Icahn School of Medicine at Mount Sinai
48	VVnr	Viral vector (Non-replicating)	Lentiviral Vector	SARS-CoV2		Theravectys – Institut Pasteur
49	VVnr	Viral vector (Non-replicating)	Lentiviral Vector	SARS-CoV2		AIOVA
50	VVnr	Viral vector (Non-replicating)	Lentiviral Vector Retro-VLP Particles	SARS-CoV2		Sorbonne University
51	VVnr	Viral vector (Non-replicating)	Ad 5 vector for intranasal administration	SARS-CoV2		University of Helsinki & University of Eastern Finland
52	VVnr	Viral vector (Non-replicating)	Oral vaccine platform	SARS-CoV2	InfA, CHIKV, LASV, NORV; EBOV, RVF, HBV, VEE	Vaxart
53	VVnr	Viral vector (Non-replicating)	Recombinant Adenovirus Vector (Type 5) + Spike protein of SARS-CoV-2	SARS-CoV2		Pasteur Institute / Iran
54	VVnr	Viral vector (Non-replicating)	Recombinant Adenovirus Vector (ChAdOx1) + Spike protein of SARS-CoV-2	SARS-CoV2		Pasteur Institute / Iran
55	VVnr	Viral vector (Non-replicating)	Adenovirus-based	SARS-CoV2		Home Iman Zist Fanavar
56	VVnr	Viral vector (Non-replicating)	Chimpanzee adenovirus vector expressing the RBD-dimer without adjuvant	SARS-CoV2		Chengdu Kanghua Biological Products Co., Ltd

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Replicating viral vector vaccines in clinical trials.

Sponsor	Location	Status	Doses	Timing of doses	Route	Age	Enrollment	Clinical Phase
University of Hong Kong, Xiamen University and Beijing Wantai Biological Pharmacy	China	Recruiting	1	ND	IN	≥18	2 group different size	Phase II (ChiCTR2000039715)
Israel Institute for Biological Research/ Weizmann Institute of Science	Israel	Recruiting	1	ND	IM	18–85	1040	Phase I/II (NCT04608305)
Shenzhen Geno-Immune Medical Institute	China	Recruiting	3	0, 14, 28 days	SC	6 Months to 80 Years	100	Phase I)NCT04299724)
Cellid Co., Ltd.	South Korea	Recruiting	1	ND	IM	19–64	150	Phase I /II) NCT04666012)
Aivita Biomedical, Inc	USA	Not yet recruiting	1	0	IM	≥18	175	Phase I /II (NCT04386252)
Mahidol University, The Government Pharmaceutical Organization	Thailand	Not yet recruiting	2	0, 28 days	IM	18–75	460	Phase I /II) NCT04764422)

COVID-19

ADENOVİRÜS VEKTÖR AŞILARI

Drug Metabolism and Pharmacokinetics 42 (2022) 100432

Contents lists available at ScienceDirect

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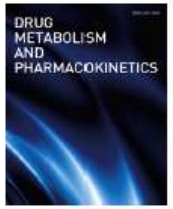


Review article

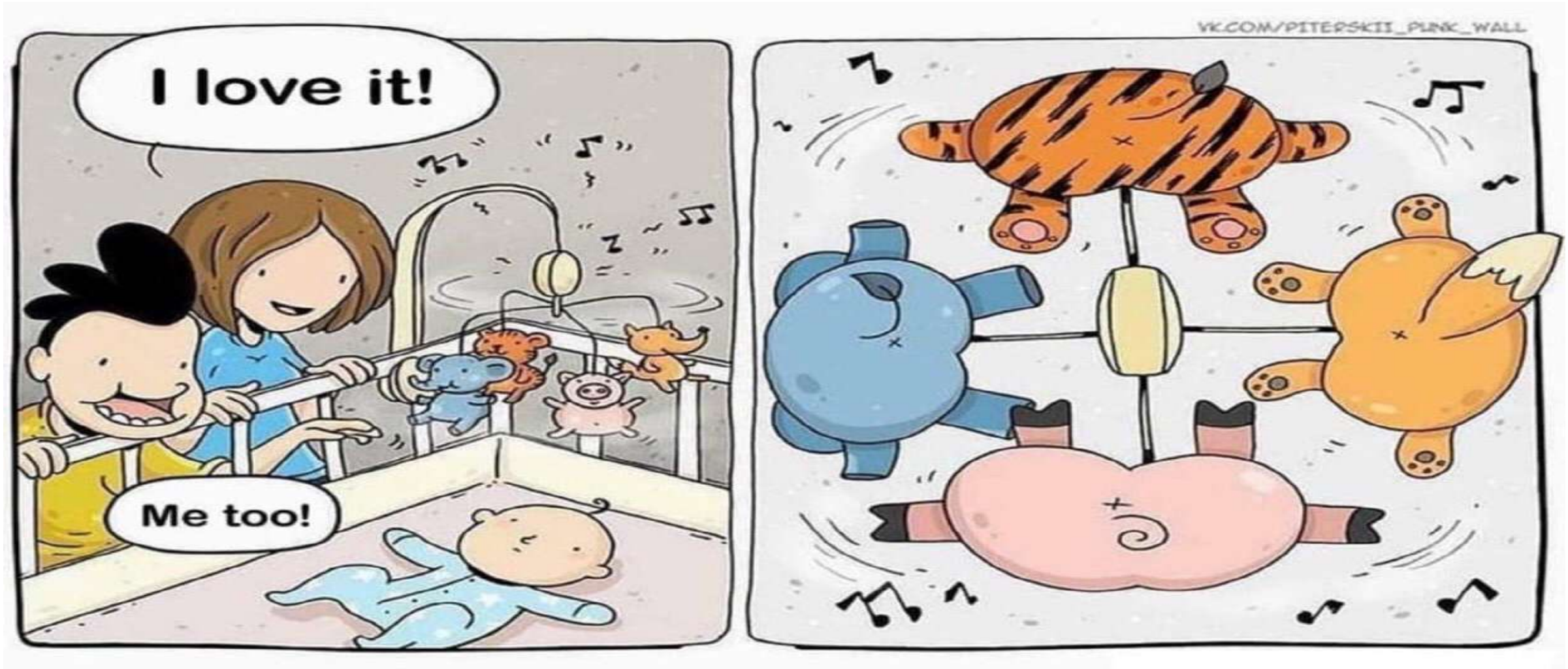
Adenovirus vector-based vaccine for infectious diseases

Fuminori Sakurai [a, *], Masashi Tachibana [b, c], Hiroyuki Mizuguchi [a, c, d, e, **]

Clinically approved Ad vector vaccines for COVID-19.

Ad vector vaccine	Developer	Type of Ads	Antigens
ChAdOx1 nCoV-19 (VAXZEVRIA, AZD1222)	AstraZeneca /University of Oxford (UK)	Chimpanzee Ad	Spike protein
Ad26.COV2-S	Johnson & Johnson (Europe)	Ad serotype 26	Spike protein
Sputnik V	Gamaleya Research Institute (Russia)	Ad serotype 26 (prime) Ad serotype 5 (boost)	Spike protein
Ad5-nCOV	CanSino Biologics Inc. (China)	Ad serotype 5	Spike protein

Sakurai et al. Drug Metabolism and Pharmacokinetics 2022



COVID-19

OXFORD VACCINE PROJECT

UNIVERSITY OF OXFORD

- 10 Ocak 2020 yeni coronavirus aşı çalışmalarına başlanmış.

- **SARS-CoV-2 spike protein**
- **ChAdOx1** (Jenner Institute)
  - Replike olmayan şempanze adenovirüs vektörü

COVID-19

AZD-1222 /VAXZEVRIA

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

Merryn Voysey, Sue Ann Costa Clemens*, Shabir A Madhi*, Lily Y Weckx*, Pedro M Folegatti*, Parvinder K Aley, Brian Angus, Vicky L Baillie, Shaun L Barnabas, Qasim E Bhorat, Sagida Bibi, Carmen Briner, Paola Cicconi, Andrea M Collins, Rachel Colin-Jones, Clare L Cutland, Thomas C Darton, Keertan Dheda, Christopher J A Duncan, Katherine R W Emary, Katie J Ewer, Lee Fairlie, Saul N Faust, Shuo Feng, Daniela M Ferreira, Adam Finn, Anna L Goodman, Catherine M Green, Christopher A Green, Paul T Heath, Catherine Hill, Helen Hill, Ian Hirsch, Susanne H C Hodgson, Alane Izu, Susan Jackson, Daniel Jenkin, Carina C D Joe, Simon Kerridge, Anthonet Koen, Gaurav Kwatra, Rajeka Lazarus, Alison M Lawrie, Alice Lelliott, Vincenzo Libri, Patrick J Lillie, Raburn Mallory, Ana V A Mendes, Eveline P Milan, Angela M Minassian, Alastair McGregor, Hazel Morrison, Yama F Mujadidi, Anusha Nana, Peter J O'Reilly, Sherman D Padayachee, Ana Pittella, Emma Plested, Katrina M Pollock, Maheshi N Ramasamy, Sarah Rhead, Alexandre V Schwarzbold, Nisha Singh, Andrew Smith, Rinn Song, Matthew D Snape, Eduardo Sprinz, Rebecca K Sutherland, Richard Tarrant, Emma C Thomson, M Estée Török, Mark Toshner, David P J Turner, Johan Vekemans, Tonya L Villafana, Marion E E Watson, Christopher J Williams, Alexander D Douglas*, Adrian V S Hill*, Teresa Lambe*, Sarah C Gilbert*, Andrew J Pollard* on behalf of the Oxford COVID Vaccine Trial Group†*

COVID-19

AZD-1222 /VAXZEVRIA

	Total number of cases	ChAdOx1 nCoV-19		Control		Vaccine efficacy (CI*)
		n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	
All LD/SD and SD/SD recipients	131	30/5807 (0·5%)	44·1 (248 299)	101/5829 (1·7%)	149·2 (247 228)	70·4% (54·8 to 80·6)†
COV002 (UK)	86	18/3744 (0·5%)	38·6 (170 369)	68/3804 (1·8%)	145·7 (170 448)	73·5% (55·5 to 84·2)
LD/SD recipients	33	3/1367 (0·2%)	14·9 (73 313)	30/1374 (2·2%)	150·2 (72 949)	90·0% (67·4 to 97·0)‡§
SD/SD recipients	53	15/2377 (0·6%)	56·4 (97 056)	38/2430 (1·6%)	142·4 (97 499)	60·3% (28·0 to 78·2)
COV003 (Brazil; all SD/SD)	45	12/2063 (0·6%)	56·2 (77 930)	33/2025 (1·6%)	157·0 (76 780)	64·2% (30·7 to 81·5)‡
All SD/SD recipients	98	27/4440 (0·6%)	56·4 (174 986)	71/4455 (1·6%)	148·8 (174 279)	62·1% (41·0 to 75·7)
Other non-primary symptomatic COVID-19 disease¶	18	7/5807 (0·1%)	10·3 (248 299)	11/5829 (0·2%)	16·3 (247 228)	36·4% (−63·8 to 75·3)‡
Any symptomatic COVID-19 disease	149	37/5807 (0·6%)	54·4 (248 299)	112/5829 (1·9%)	165·5 (247 228)	67·1% (52·3 to 77·3)
Asymptomatic or symptoms unknown (COV002)	69	29/3288 (0·9%)	69·8 (151 673)	40/3350 (1·2%)	96·0 (152 138)	27·3% (−17·2 to 54·9)
LD/SD recipients	24	7/1120 (0·6%)	41·4 (61 782)	17/1127 (1·5%)	100·6 (61 730)	58·9% (1·0 to 82·9)‡
SD/SD recipients	45	22/2168 (1·0%)	89·4 (89 891)	23/2223 (1·0%)	92·9 (90 408)	3·8% (−72·4 to 46·3)
Any NAAT-positive swab	221	68/5807 (1·2%)	100·0 (248 299)	153/5829 (2·6%)	226·0 (247 228)	55·7% (41·1 to 66·7)

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ETKİNLİK %62-90

Voysey M et al. Lancet 2021

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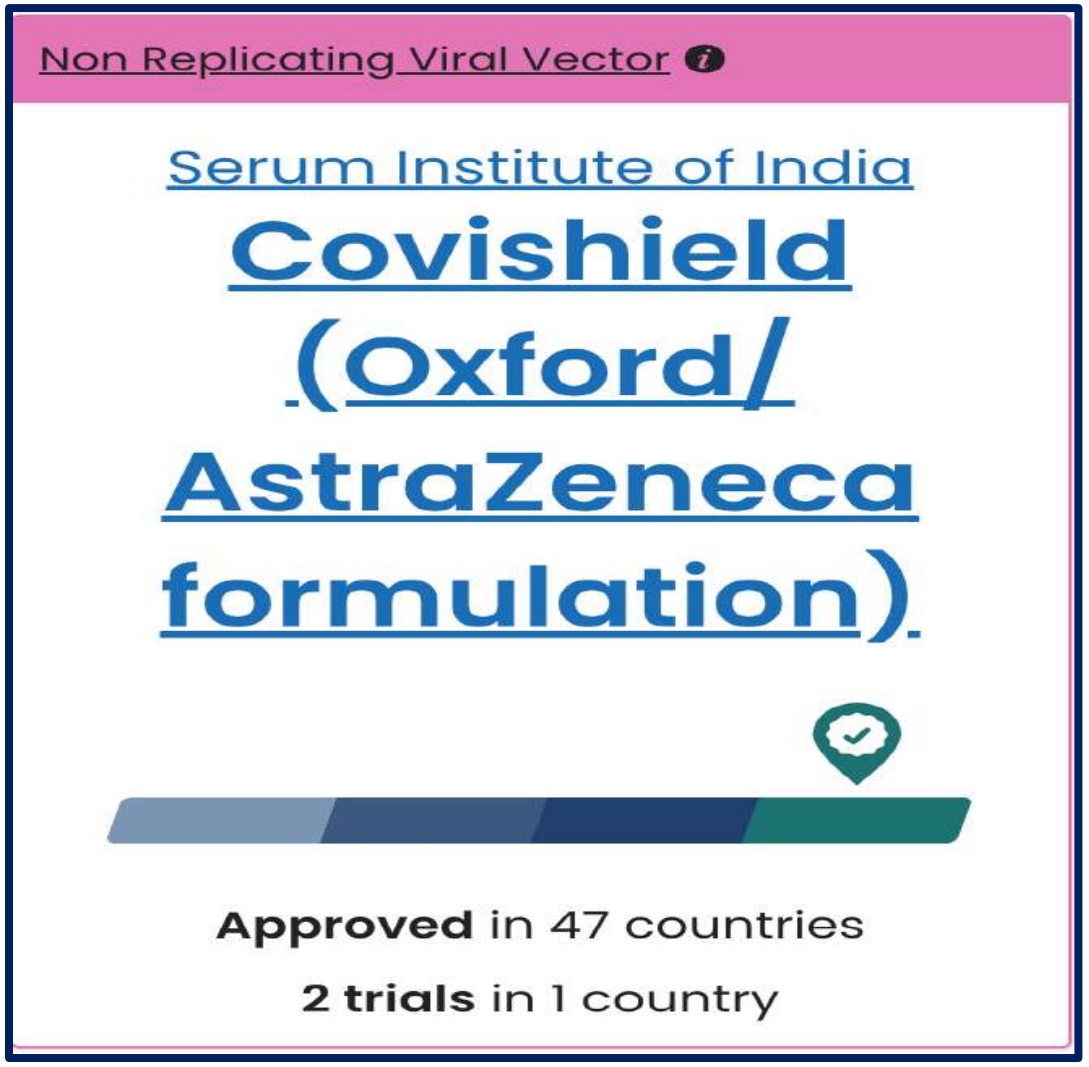

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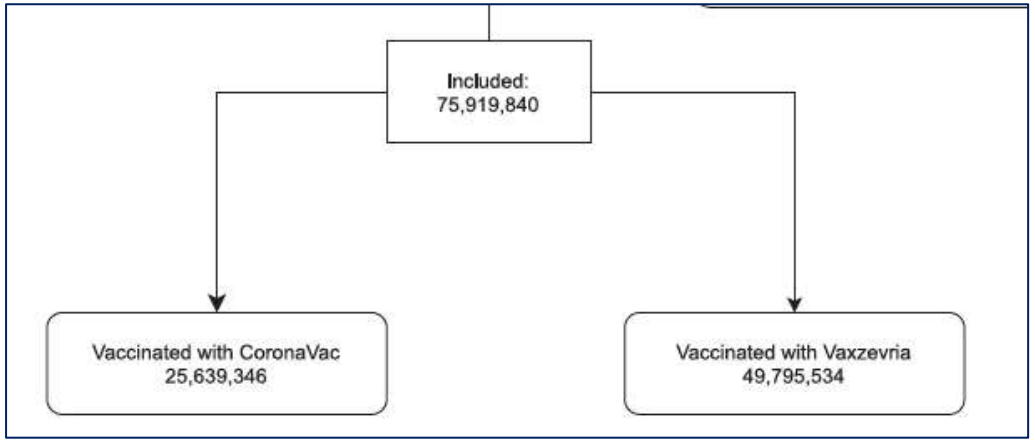
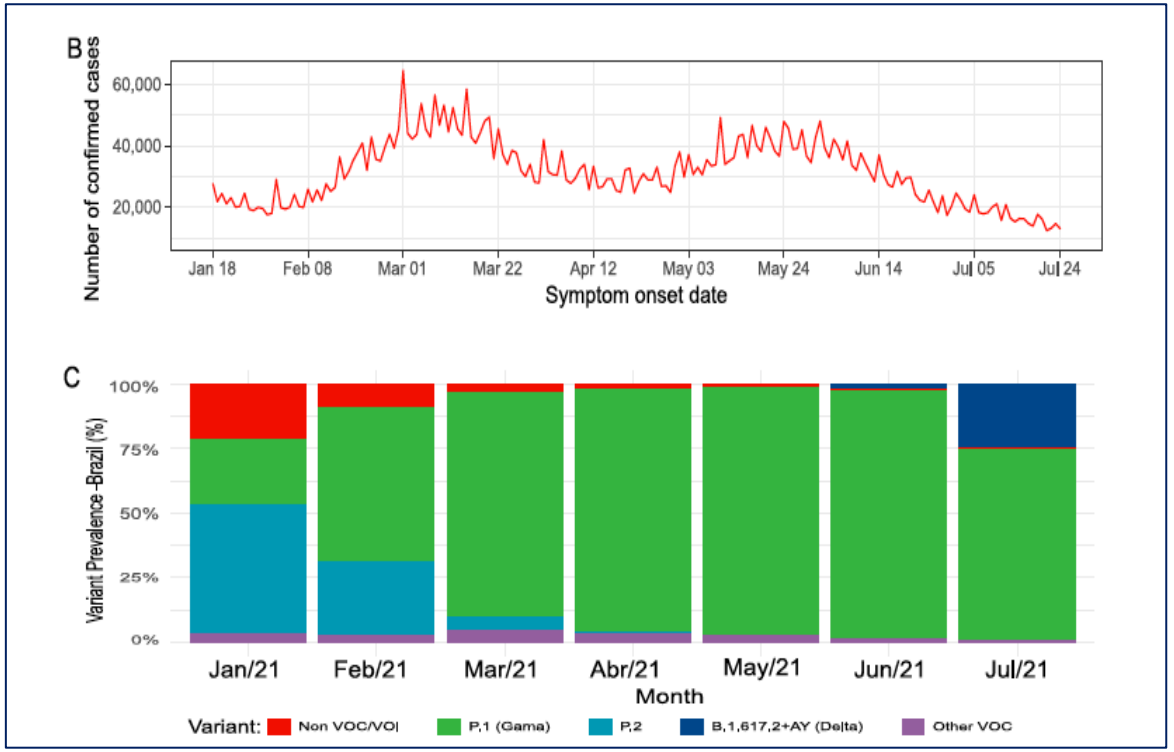
AZD-1222 /VAXZEVRIA

Influence of age on the effectiveness and duration of protection of Vaxzevria and CoronaVac vaccines: A population-based study

*Thiago Cerqueira-Silva,[ab,1] Vinicius de Araújo Oliveira,[ab,c,1] Viviane S. Boaventura,[a,b,1] Julia M. Pescarini,[c,d] Juracy Bertoldo Júnior,[b,c] Tales Mota Machado,[e] Renzo Flores-Ortiz,[c] Gerson O. Penna,[f] Maria Yury Ichihara,[c] Jacson Venâncio de Barros,[g] Mauricio L. Barreto,[b,c] Guilherme Loureiro Werneck,[h] and Manoel Barral-Netto[a,b,c]**





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AZD-1222 /VAXZEVRIA

	Vaxzevria/Fiocruz				CoronaVac/Butantan			
	Person-years	Events	Incidence per 100 person-years	VE% (95% CI)*	Person-years	Events	Incidence per 100 person-years	VE% (95% CI)*
Infection								
Reference period	1 662 565·5	130,302	7·84	Ref	855,542·2	68,126	7·96	Ref
Partially vaccinated	5 550 664·6	247,799	4·46	50·4 (49·6–51·1)	1,290,469·1	74,895	5·80	28·7 (27.1–30.2)
Fully vaccinated	572 003·4	14,771	2·58	78·1 (77·2–79·0)	4,574,691·4	194,864	4·26	53·2 (52·4–54·1)
Hospitalization								
Reference period	1,664,388·0	22,449	1·35	Ref	856,418·3	16,289	1·90	Ref
Partially vaccinated	5,587,966·0	28,713	0·51	70.9 (69·7–72·1)	1,303,567·1	15,076	1·16	38·4 (35·5–41·2)
Fully vaccinated	580,979·1	1292	0·22	91.4 (90·1–92·5)	4,624,347·6	28,810	0·62	71.2 (70·0–72·4)
ICU admission								
Reference period	1,664,660·2	7558	0·45	Ref	856,597·5	6008	0·70	Ref
Partially vaccinated	5,592,952·5	9907	0·18	71·0 (69·0–73·0)	1,307,124·7	5560	0·43	39·6 (34·8–44·0)
Fully vaccinated	581,594·0	477	0·08	91·1 (88·9–92·9)	4,629,831·8	10,364	0·22	72·2 (70·2 – 74·0)
Death								
Reference period	1,664,670·8	7037	0·42	Ref	856,563·2	7852	0·92	Ref
Partially vaccinated	5,592,331·8	10,579	0·19	69·7 (67·5–71·8)	1,305,706·9	7203	0·55	39·0 (34·9–42·9)
Fully vaccinated	581,648·9	564	0·10	92·3 (90·5–93·7)	4,629,255·8	13,166	0·28	73·7 (72·1–75·2)

***Table 1*: Vaccine effectiveness in adults partially and fully vaccinated[+] with Vaxzevria and CoronaVac for COVID-19 infection, hospitalization, ICU admission, and death. Brazil, 2021.**

[+] Reference period: ≤13 days after the first dose; Partially vaccinated: ≥14 days after the first dose and without the second dose; Fully vaccinated: ≥14 days after the second dose. ICU denotes intensive care unit.

* Negative binomial model adjusted for age, sex, region of residence, month of administration of first dose, municipal deprivation level and Effective Reproductive Number (Rt).

VİRAL VEKTÖR AŞILARI

AZD-1222 /VAXZEVRIA

Vaccine	Outcome	No. of Studies Included	Participants, No.	Pooled Diagnostic Odds Ratio [DOR] (95% CI)	I^2 test for heterogeneity, %	Vaccine Effectiveness, % (95% CI)[a]
mRNA or viral vector	Infection	10	16,456,882	0.158 (0.157–0.160)	0	84.2 (84.0–84.3)
Pfizer/BioNTech	Infection	5	15,575,120	0.185 (0.184–0.187)	0	81.5 (81.3–81.6)
mRNA or viral vector	Infection during the δ variant period	4	11,476,256	0.388 (0.367–0.410)	0	61.2 (59.0–63.3)
mRNA or other vaccines	Hospitalization	8	3,194,708	0.113 (0.029–0.442)	0	88.7 (55.8–97.1)
Pfizer/BioNTech	Hospitalization	6	1,133,521	0.146 (0.140–0.152)	51	85.4 (84.8–86.0)
Moderna	Hospitalization	5	142,981	0.102 (0.096–0.108)	32	89.8 (89.2–90.4)

Antimicrobial Stewardship & Healthcare Epidemiology (2022), **2**, e22, 1–12
doi:10.1017/ash.2021.261

SHEA

Review

The long-term effectiveness of coronavirus disease 2019 (COVID-19) vaccines: A systematic literature review and meta-analysis

AŞI YANITI ÜZERİNE ETKİLİ FAKTÖRLER

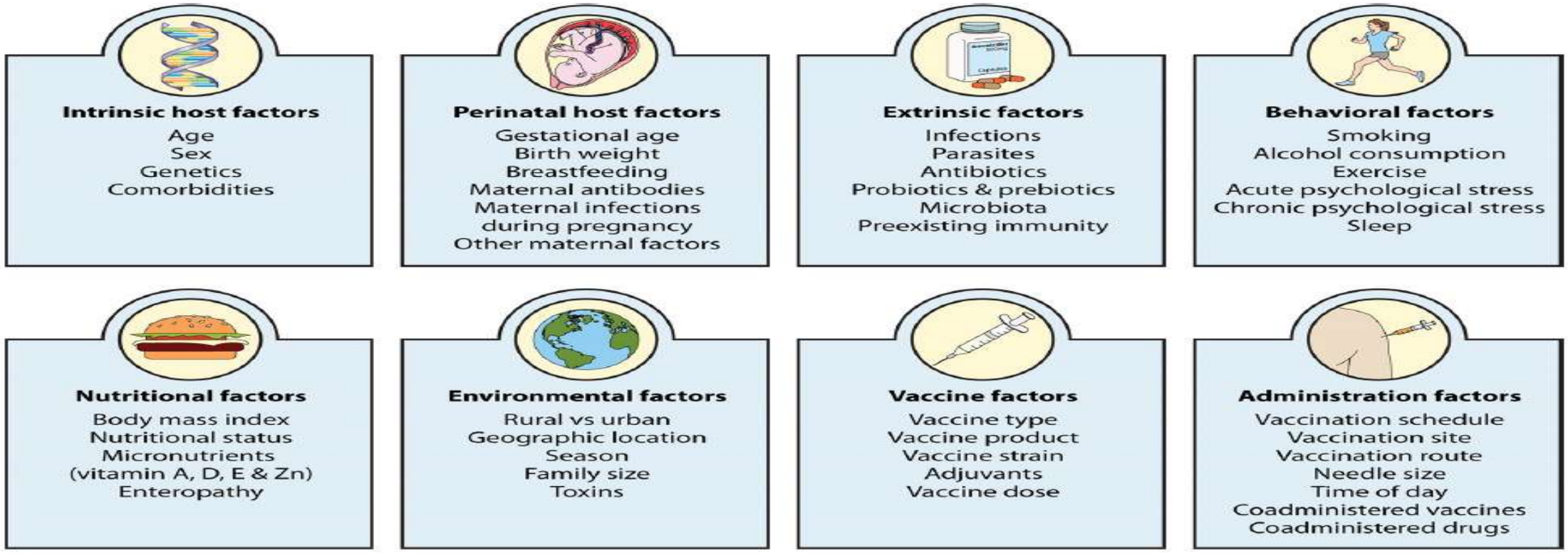


FIG 1 Factors that influence the immune response to vaccination.

AMERICAN SOCIETY FOR MICROBIOLOGY | Clinical Microbiology Reviews®

REVIEW

Factors That Influence the Immune Response to Vaccination

Petra Zimmermann,[a,b,c,d,e] Nigel Curtis[a,b,c]

COVID-19

AZD-1222 /VAXZEVRIA

- Aralık 2020'de İngiltere'de acil kullanım onayı aldı.
- Hastaneye yatış gerektiren enfeksiyonda **%80 azalma**
- 6 hafta ara ile 2 doz uygulama %55, **12 hafta ara ile 2 doz uygulama %81**
- 28-34 gün ara ile aşılamada hastanede yatış %94 ↓ (80 yaş üzerinde %81 ↓)
- **15 Şubat 2021 WHO-EUL** (yaşlılarda etkinin azalmış olduğu uyarısı ile)
- ABD'de başvurusu yok (FDA)
- Alfa varyantından koruyuculuğu iyi olmakla birlikte, beta varyantından (Güney Afrika) koruma %10 (nötralizasyon antikor yanıtı beta varyantında 9 kat ↓
- İlk doz alfa etkililiği %48.7, delta etkililiği %30.7
- İkinci dozda alfa için %74.5, delta etkililiği %67

COVID-19

AZD-1222 /VAXZEVRIA

- Tromboembolik olay (Mart 2021)
- EMEA uyarısı 5 milyon kişide 30 venöz tromboemboli
  - 32-54 yaş arası
  - Platelet faktör 4 antikorları (heparin ilişkili trombositopeni gibi ama heparin kullanım öyküsü yok)
  - **VACCINE INDUCED IMMUNE THROMBOTIC THROMBOCYTOPENIA**
- C terminaline yer alan solubl spike protein varynatları (endotelde ACE-2 reseptörlerine bağlanma)
  - Vaccine-induced COVID-19 mimicry syndrome (VIC19M syndrome).

International Immunopharmacology 100 (2021) 108162

COVID-19

AZD-1222 /VAXZEVRIA

- EMEA aşı sonrası 2 hafta içerisinde tromboemboli riski artışı tanımlamış ama fayda-zarar dengesi **fayda yönünde** değerlendirilmiş.

- 8 Eylül 2021 EMEA
  - Tromboz-trombositopeni olguları (592 milyon uygulamada 1503 olgu).
  - Guillain Barre sendromu uyarısı (592 milyon uygulamada 883 olgu)
  - Nadiren kapiller kaçak sendromu
  - Serebral ven trombozu (trombositopeni olmaksızın)
  - Karın ağrısı, kol ve bacaklarda soğuma, influenza benzeri bulgular
  - Menstrüel bozukluklar ile ilişki gösterilmemiştir.

International Immunopharmacology 100 (2021) 108162

COVID-19

JANNSEN ADV26 AŞISI

Non Replicating Viral Vector

Janssen (Johnson & Johnson)

Ad26.COV2.S

Approved in 106 countries

18 trials in 18 countries

RESEARCH SUMMARY

Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19

Sadoff J et al. DOI: 10.1056/NEJMoa2101544

BACKGROUND

Vaccines are needed to control the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. Safe adenovirus vector-based vaccines have induced durable immune responses to other diseases.

CLINICAL TRIAL

Design: A randomized, double-blind trial to evaluate the safety and efficacy of Ad26.COV2.S, a recombinant, replication-incompetent human adenovirus 26 vector encoding a full-length membrane-bound SARS-CoV-2 spike protein.

Intervention: 19,630 participants ≥18 years old were assigned to receive a single intramuscular dose of Ad26.COV2.S, and 19,691 were assigned to placebo. Participants were monitored for safety and for the occurrence of moderate to severe–critical Covid-19 with onset ≥14 days and ≥28 days after injection.

RESULTS

Efficacy: The incidence of moderate to severe–critical Covid-19 with onset ≥14 days and ≥28 days was lower among vaccine recipients. The incidences of severe–critical Covid-19 (including incidence in South Africa, despite high prevalence of the 20H/501Y.V2, or B.1.351, variant), hospitalization, and death were lower with vaccine than with placebo.

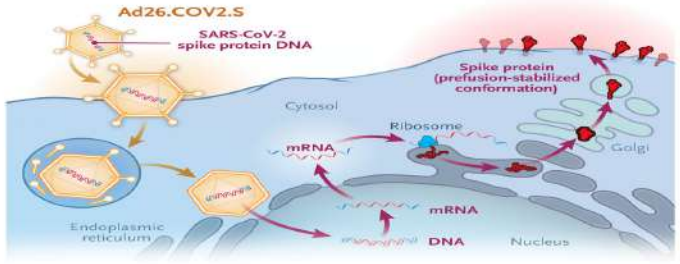
Safety: Vaccine recipients were more likely to have reactogenicity, mostly injection-site pain, as well as systemic symptoms of headache, fatigue, myalgia, or nausea. Most symptoms were mild to moderate in severity and lasted 1 to 2 days.

LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- Safety and efficacy of Ad26.COV2.S in children.
- Long-term safety and efficacy and whether the vaccine protects against asymptomatic transmission.
- Efficacy against emerging SARS-CoV-2 variants.

Links: Full article | NEJM Quick Take



Solicited Local Adverse Events Reported within 7 days after the Administration of Vaccine or Placebo (Safety Subpopulation).

Variable	≥14 Days after Administration				
	Ad26.COV2.S (N = 19,514)		Placebo (N = 19,544)		Vaccine Efficacy (95% CI)
	no. of cases	person-yr	no. of cases	person-yr	%
Moderate to severe–critical Covid-19	116	3116.6	348	3096.1	66.9 (59.0–73.4)
18–59 yr	95	2106.8	260	2095.0	63.7 (53.9–71.6)
≥60 yr	21	1009.8	88	1001.2	76.3 (61.6–86.0)
Variable	**≥28 Days after Administration**				
Moderate to severe–critical Covid-19	66	3102.0	193	3070.7	66.1 (55.0–74.8)
18–59 yr	52	2097.6	152	2077.0	66.1 (53.3–75.8)
≥60 yr	14	1004.4	41	993.6	66.2 (36.7–83.0)

CONCLUSIONS

A single dose of Ad26.COV2.S was safe and efficacious against symptomatic Covid-19.

Spike protein ile vektör olarak Adenovirüs 26 (replike olmayan)

ener çağrı dinleyici

COVID-19

Ad26.COV2-S

- Tek doz aşı uygulaması ile aşılananarın %90'ında antikor yanıtı
- Tek doz aşı uygulaması ile orta-ağır enfeksiyondan %66 koruma, hastaneye yatış ve ölümden %100 korunma
- FDA, EUA onayı
- Alfa, beta, gamma, epsilon etkili.
- Splanik ven trombozu, serebral ven trombozu, derin ven trombozu
- 6.8 milyon doz uygulamada 6 olgu (18-48 yaş kadınlar) aşı uygulaması durduruldu.
- Tromboz ve trombositopeni aşılamadan 6-13 gün sonrasında oluyor.
- Yeniden kullanım izni, aşıdan 3 hafta içerisinde semptom takibi

COVID-19

ADENOVİRÜS AŞILARI GÜVENLİK

American Journal of Emergency Medicine 49 (2021) 58–61

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Reviews

Thrombosis with thrombocytopenia syndrome associated with COVID-19 vaccines

Brit Long, M.D.[a,1,*], Rachel Bridwell, M.D.[a], Michael Gottlieb, M.D.[b]

TTS definition, recommended testing, and management [11,12].

Definition	1) Exposure to the ChAdOx1 nCoV-19 or AD26.COV2·S vaccine 4–30 days prior to presentation 2) Thrombosis (arterial or venous) 3) Thrombocytopenia ($<150 \times 10^9$/L) 4) Positive PF4-heparin ELISAPresume TTS in patients with signs and symptoms of serious thrombosis and one of the following: positive imaging, thrombocytopenia, or both
Recommended evaluation	CBC, peripheral smear, D-dimer, fibrinogen, coagulation panel, PF4-heparin ELISA; imaging based on assessment
Management	1) IVIG 1–2 g/kg/day for 2 days 2) Anticoagulation: argatroban or bivalirudin first line 3) Avoid heparin, platelet transfusion, antiplatelet therapies

PF4-heparin ELISA, platelet factor 4-heparin enzyme-linked immunosorbent assay; TTS, thrombosis with thrombocytopenia syndrome; CBC, complete blood count; IVIG, intravenous immunoglobulin.

Comparison of TTS with ChAdOx1 nCoV-19 vaccine and AD26.COV2·S vaccine [11].

Characteristic	ChAdOx1 nCoV-19 vaccine cases	AD26.COV2·S vaccine cases
Total cases	246 CVT; 150 other locations	12 CVT; 11 other locations
Age	21–77 years	18–59 years
Gender (female to male ratio)	2.5:1	15:0
Symptoms	Headache, backache, abdominal pain, visual disturbance, leg/arm weakness	Headache, lethargy, back pain, abdominal pain, neurologic symptoms
Thrombosis	Cerebral veins, splanchnic veins, DVT/PE, arterial thrombosis	Cerebral veins, splanchnic veins
Platelet nadir	$7–113{,}000 \times 10^9$/L	$10–127{,}000 \times 10^9$/L
Platelet factor 4-heparin assay	Positive	Positive

Long et al. Am J Emerg Med 2021

COVID-19

Gam-COVID-Vac (Gamaleya, Sputnik)

Non Replicating Viral Vector

Gamaleya

Sputnik Light

Approved in 26 countries

4 trials in 2 countries

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia

Denis Y Logunov*, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatullin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg

COVID-19

Gam-COVID-Vac (Gamaleya, Sputnik)

Non Replicating Viral Vector

Gamaleya

Sputnik V

Approved in 74 countries

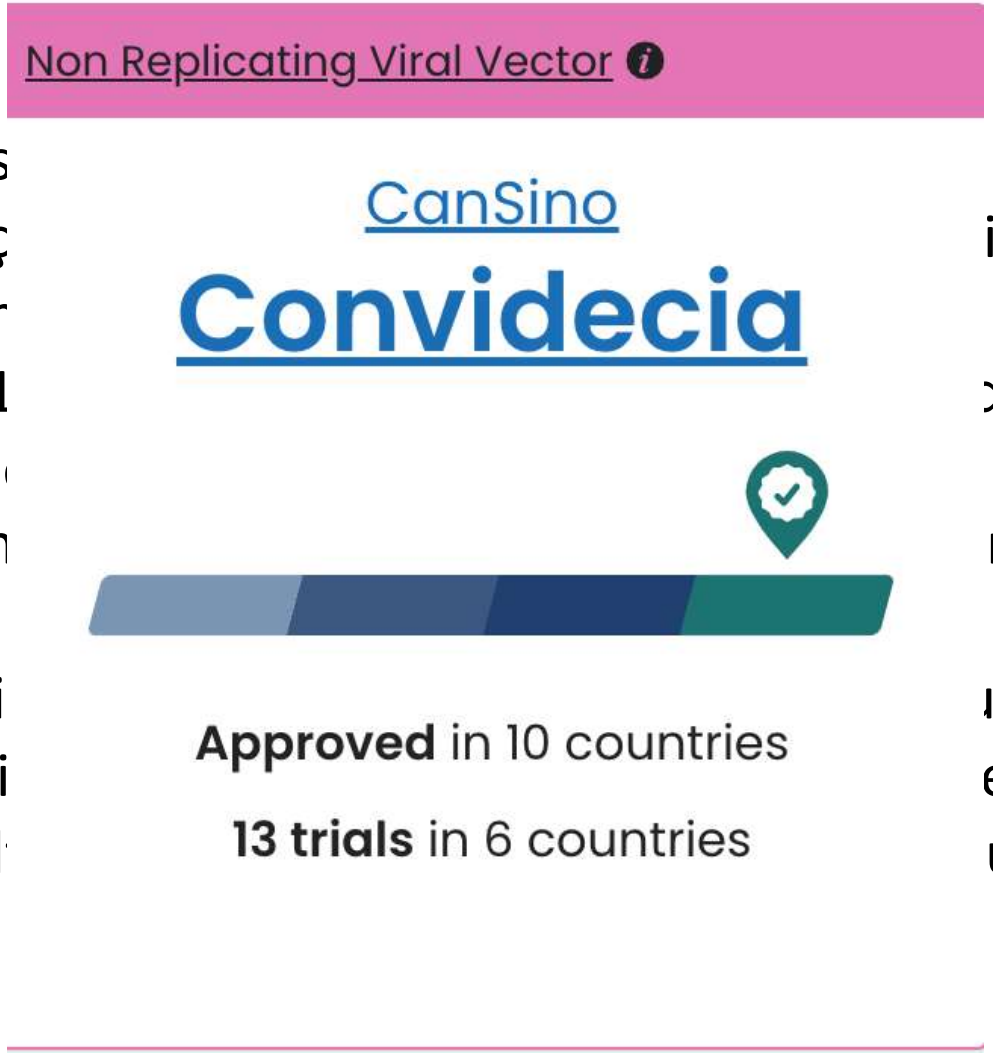
22 trials in 7 countries

*Dave Granlund

ener çağrı dinleyici

COVID-19

Ad5-nCoV (CanSino)



- Adenovirüs 5 vektör aşıs
- Erken Faz 1 çalışması (aç ilmiş ve tek doz aşı sonrasında humoral ve h
- Faz 2 çalışmasında (5 × 1 da antikor yanıtının yetersiz olması nedeni il
- Aşınının mukozal immün rlikte mukozal uygulama değerlendiriliyor.
- Hayvan çalışmalarında, i ukozal uygulamanın üst ve alt solunum yolu enfeksi etkili olduğu gösterilmiş (kişiler arası bulaşın azal uçlar henüz gösterilmedi.

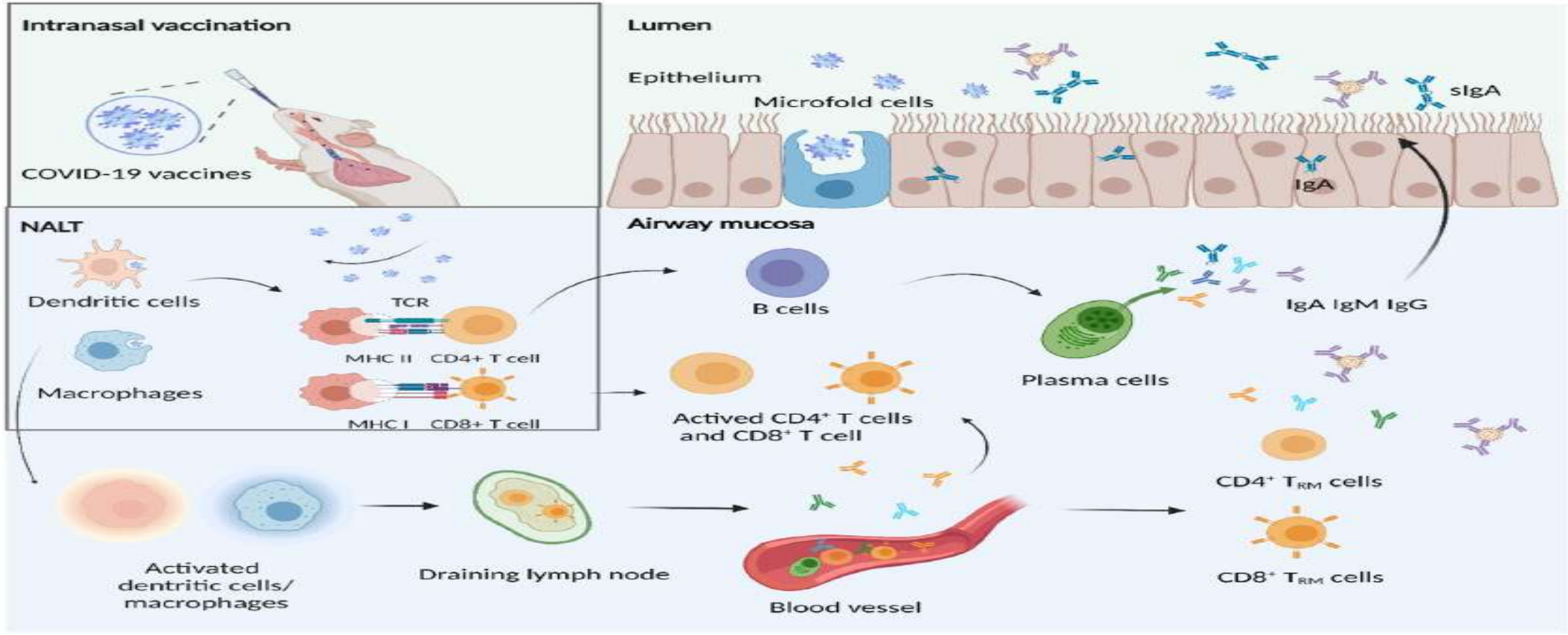
FARKLI AŞILARI KARŞILAŞTIRILMASI

VİRAL VEKTÖR AŞILARI-COVID19-ÇOCUK

Merlin Coles, 3, watches horse racing at Royal Ascot from his home in Bere Regis, England, on June 17. The boy is sitting on his horse, Mr. Glitter Sparkles, with his dog, Mistress, as racing resumed behind closed doors.
Paul Childs—Reuters

VİRAL VEKTÖR AŞILARI

İNTRANAZAL AŞILAR



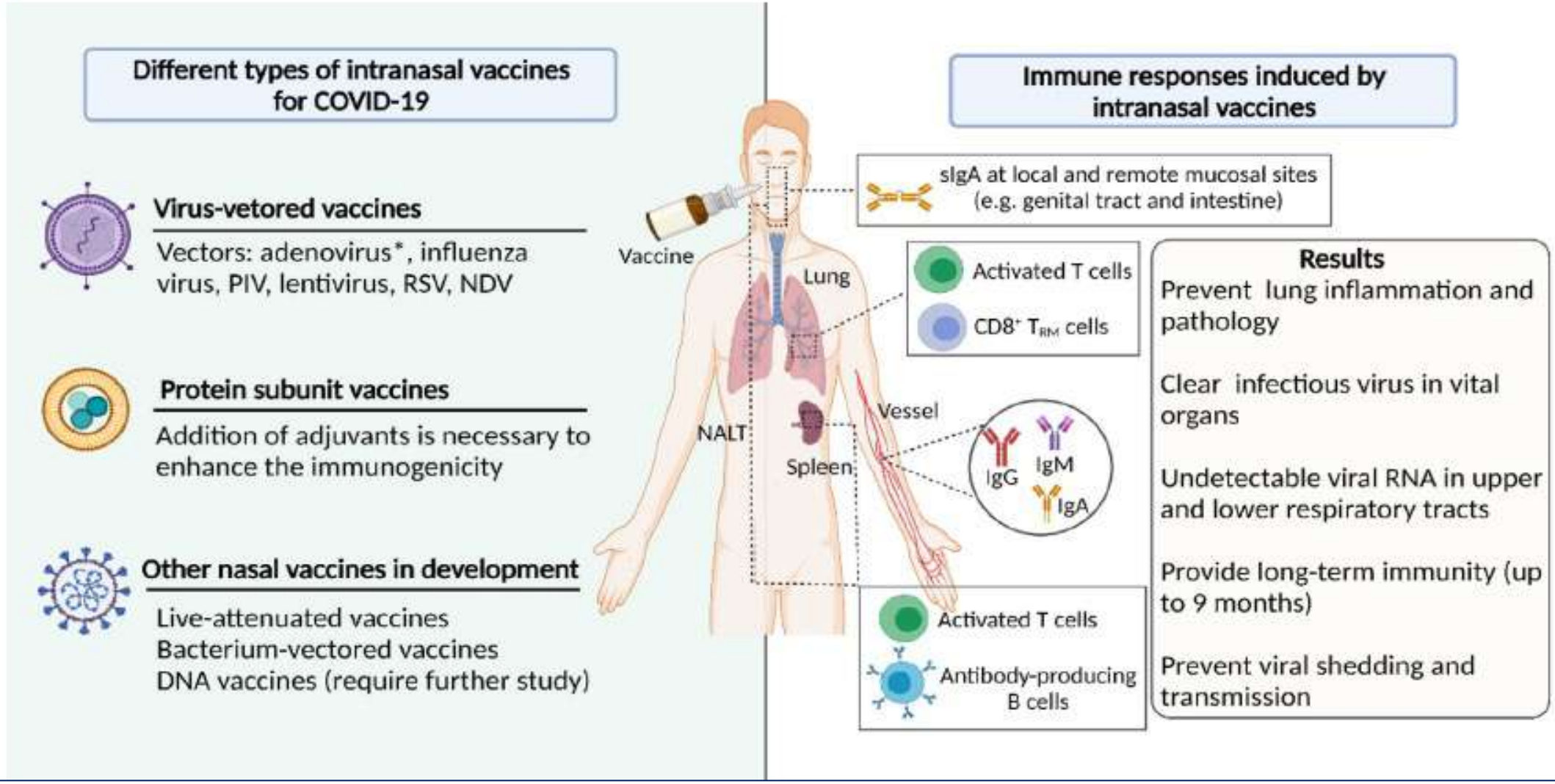
Intranasal COVID-19 vaccines: From bench to bed

Aqu Alu,[1] Li Chen,[1] Hong Lei Yuquan Wei Xiaohe Tian, and Xiawei Wei **

Laboratory of Aging Research and Cancer Drug Target, State Key Laboratory of Biotherapy and Cancer Center, National Clinical Research Center for Geriatrics, West China Hospital, Sichuan University, Chengdu 610041, China

VİRAL VEKTÖR AŞILARI

İNTRANAZAL AŞILAR



VİRAL VEKTÖR AŞILARI

İNTRANAZAL AŞILAR

Type	Vaccine	Target	Route (no. of doses)	Animal used
PIV5-vectored vaccine	CVXGA1	S protein	IN (1)	K18-hACE2 mice and ferrets[55]
hPIV2-vectored vaccine	BCPIV/S-2PM	S protein	IN (1or 2)	Mice and golden hamsters[56]
NDV-vectored vaccine	AVX/COVID-12-HEXAPRO	S protein	IN +IN, IM + IM, or IN + IM, (2)	Mice, hamsters[60], and pigs[59]
	NDV-FLS	S protein	IN (1 or 2)	Hamsters[61]
	rNDV-S	S protein	IN (2)	Mice and hamsters[62]
VSV-vectored vaccine	rVSVSARS-CoV-2	S protein	IN or IM, (1)	Normal/hACE2 mice, and macaques[63]
	VSV-SARS2-EBOV	SARS-CoV-2 S protein and/or the EBOV glycoprotein	IM or IN, (1)	Hamsters[64] and rhesus macaques[65]
Virus like particles		RBD protein	IM alone or IM + IN, (3)	Ferrets[72]
Live-attenuated vaccine	SARS-CoV-2/ human/ Korea/ CNUHV03-CA22 ℃ /2020		IN spray (1)	hACE2 transgenic mice[76]
	COVI-VAC		IN (1)	Syrian golden hamsters[77]
Bacterium-vectored vaccine		M and N proteins	ID or IN, (2)	Hamsters[78]
	LP18:RBD	RBD	IN (2)	Mice[79]
Protein subunit vaccine		RBD protein	IN, IM or ID, (3)	Mice[34]
		S1 protein	IM (3) or IN (4)	Rhesus macaques[73]
		RBD protein	IN or IM, (3)	Mice[69]
		S1 protein	IN (3)	Mice[70]
		Trimeric or monomeric S protein	IN (1)	Mice[71]
DNA vaccine	pQAC—CoV; MVA-CoV	S and N proteins	IN or IM, (3), or IN (2)	Mice[81]
		S protein	IN	Mice[80]

VİRAL VEKTÖR AŞILARI

İNTRANAZAL AŞILAR

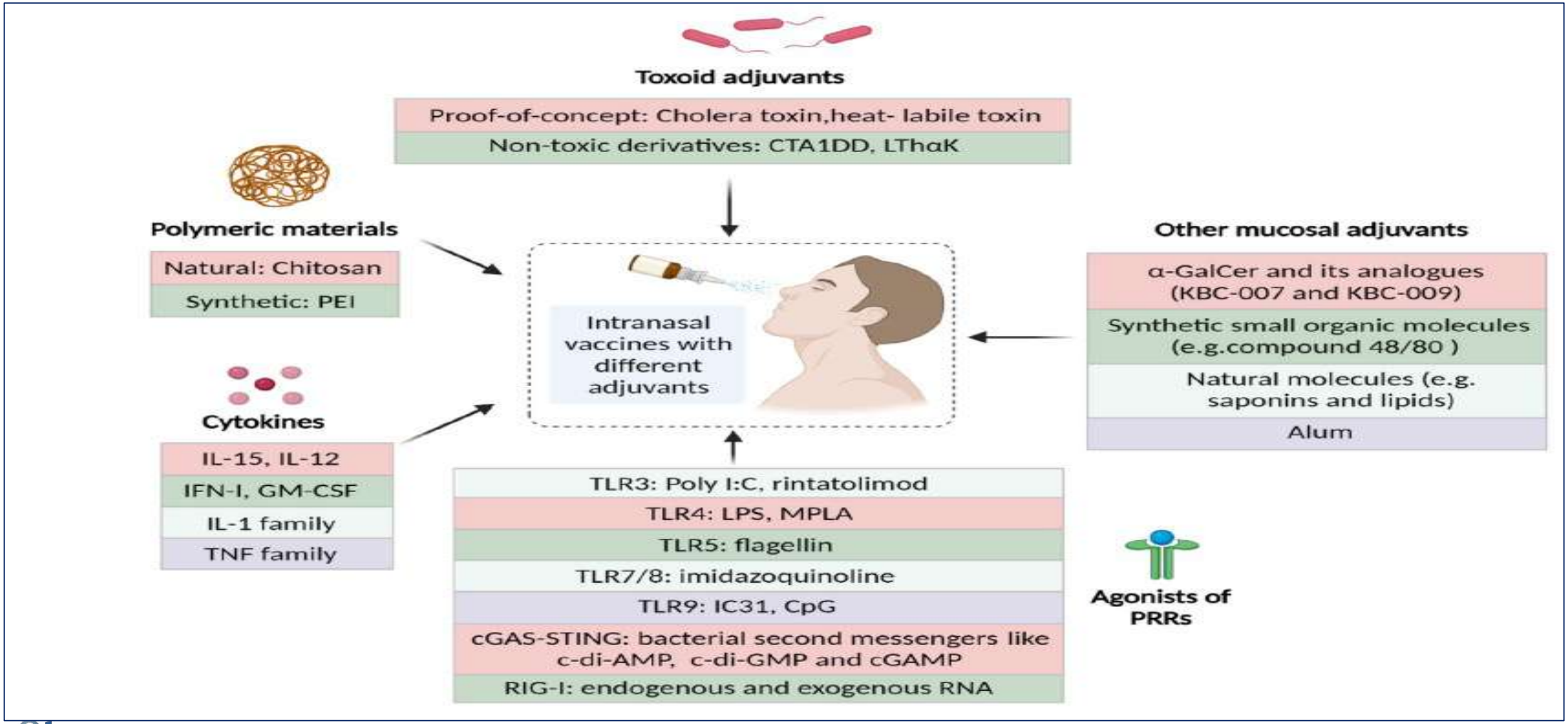
Type	Vaccine	Developer/manufacturer	Nasal delivery device	Phase	Status	Enrollment	Clinical trial No.	Route
Ad-vectored vaccine	Ad5-nCoV	CanSino/Beijing Institute of Biotechnology	Aerogen Ultra Device	I	Active, not recruiting	149	NCT04552366	IN, IM or IN+IM
				I/II	Recruiting	840	NCT04840992	IM or IN
	ChAdOx1	AstraZeneca/University of Oxford	MAD Nasal™ Intranasal Mucosal Atomization Device	I	Enrolling by invitation	54	NCT04816019	IN
	BBV154	Bharat Biotech International Limited	N/A	I	Active, not recruiting	175	NCT04751682	IN
	SC-Ad6–1	Tetherex Pharmaceuticals Corporation	N/A	I	Recruiting	80	NCT04839042	IM or IN
	AdCOVID	Altimmune, Inc.	Pipette droppers	I	Not processing	180	NCT04679909	IN
NDV-vectored vaccine	AVX/COVID-12-HEXAPRO	Laboratorio Avi-Mex, S.A. de C.V.	An automatic syringe (Prima mist sprayer)	I	Recruiting	90	NCT04871737	IN, IM or IN+IM
LAIV-vectored vaccine	DelNS1–2019-nCoV-RBD-OPT1	University of Hong Kong, Xiamen University and Beijing Wantai Biological Pharmacy	Spray devices	I	Complete	60	ChiCTR2000037782	IN
				II	Complete	720	ChiCTR2000039715	IN
				III	–	40,000	ChiCTR2100051391	IN
PIV5-vectored vaccine	CVXGA1	CyanVac LLC	Spray devices	I	Not recruiting	80	NCT04954287	IN
RSV-vectored vaccine	MV-014–212	Meissa Vaccines, Inc.	Droppers or spray devices	I	Recruiting	130	NCT04798001	IN
Protein subunit vaccine	CIGB-669	CIGB	Syringe-based spray devices	I/II	Pending	88	RPCEC00000345	IN alone or IN + IM
	Razi Cov Pars	Razi Vaccine and Serum Research Institute	Spray devices	I	Complete	133	IRCT20201214049709N1	IM + IN
				II	Complete	500	IRCT20201214049709N2	IM + IN
				III	–	41,128	IRCT20210206050259N3	IM + IN
Live attenuated vaccine	COVI-VAC	Codagenix, Inc.	Droppers	I	Active, not recruiting	48	NCT04619628	IN

***Table 2*: Clinical trials of IN COVID-19 vaccines.**

NDV: Newcastle disease virus; LAIV: live attenuated influenza virus; PIV: parainfluenza virus; RSV: respiratory syncytial virus; N/A: Not available. Data from https://clinicaltrials.gov/, https://www.chictr.org.cn/index.aspx and https://covid-19.cochrane.org/.

VİRAL VEKTÖR AŞILARI

İNTRANAZAL AŞILAR



ALL BAD THINGS MUST COME TO AN END.

VİRAL VEKTÖR AŞILARI

Kızamık Virüs Vektör

- Kızamık virüsü sitoplazma içerisinde replike olan, konakçı kromozomuna entegre olma potansiyeli yok.
- Genetik stabilitesi yüksek, düşük ücretle yüksek doz üretme potansiyeli mevcut.
- Attenüe kızamık suşu ile MERS ve SARS-CoV çalışmalarında olumlu sonuçlar
- Daha önceden kızamık hastalığına ya da aşısına bağlı mevcut immünitenin, yeni aşı adayının immunolojik yanıtına etkisi olmamış (*Chikungunya-MV-based*)
- Schwartz kızamık suşu
- Ağustos 2020'de Fransa ve Belçika'da SARS-CoV-2 aşısı Faz 1-2 (V591-001- Measles-vector based (TMVo38)

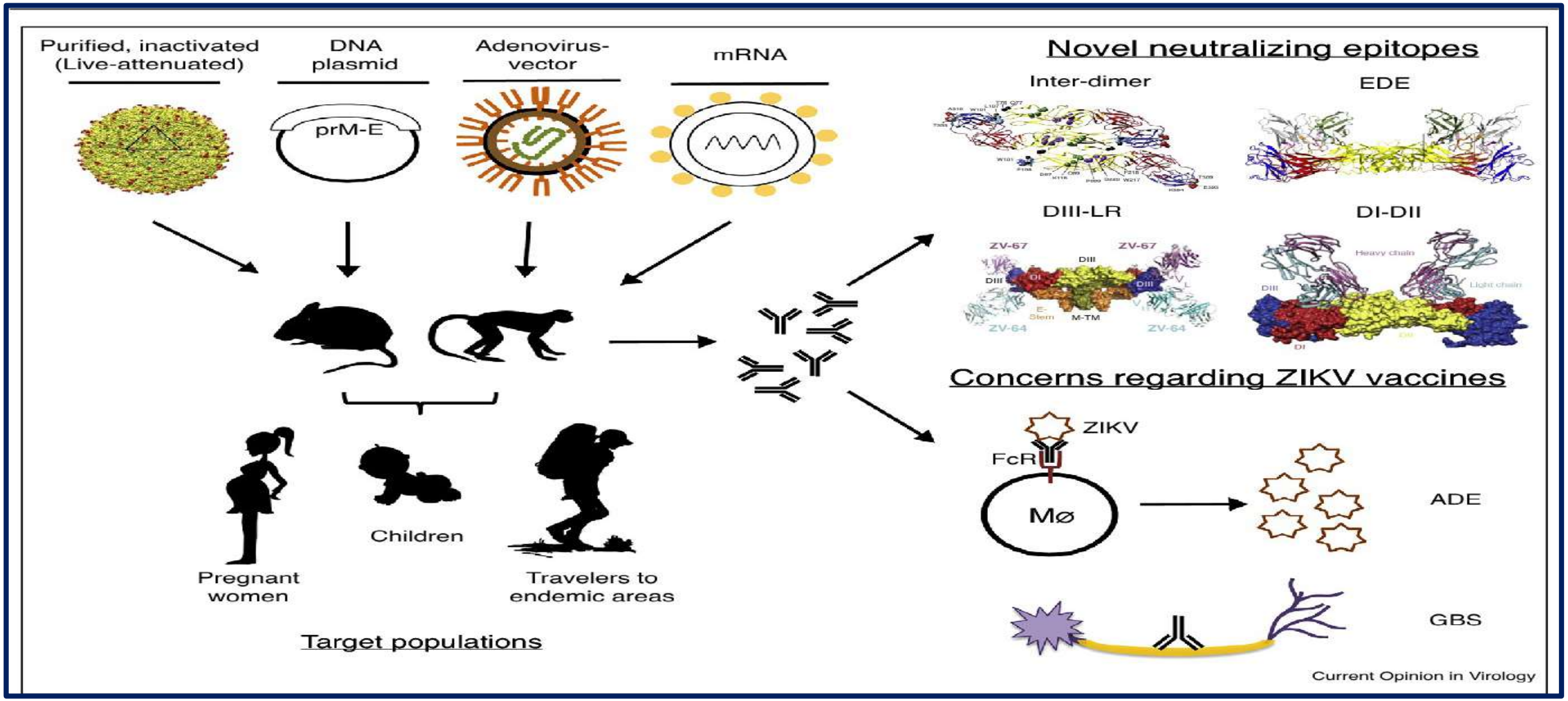
VİRAL VEKTÖR AŞILARI

Newcastle Disease Virüs Vektör

- Rekombinant Newcastle disease virus (NDV) vektörü
- İnsan ve kanatlı kaynaklı ciddi enfeksiyonlarda ümit veren sonuçlar mevcut
- Daha önceden geçirilmiş enfeksiyona ait immünite olasılığı çok düşük.
- Afrika'da SARS-COV-NDV aşı adayı ile yapılan deneysel çalışmalarda yüksek nötralizan antikor yanıtı
- Inactivated SARS-COV-2-NDV-based vaccine: Deneysel çalışmalarda antikor yanıtı iyi.
- Avantajı, etkin aşı geliştirilmesi durumunda düşük maliyet ile yüksek doz üretim olanağı

VİRAL VEKTÖR AŞILARI

ZİKAVİRÜS AŞILARI



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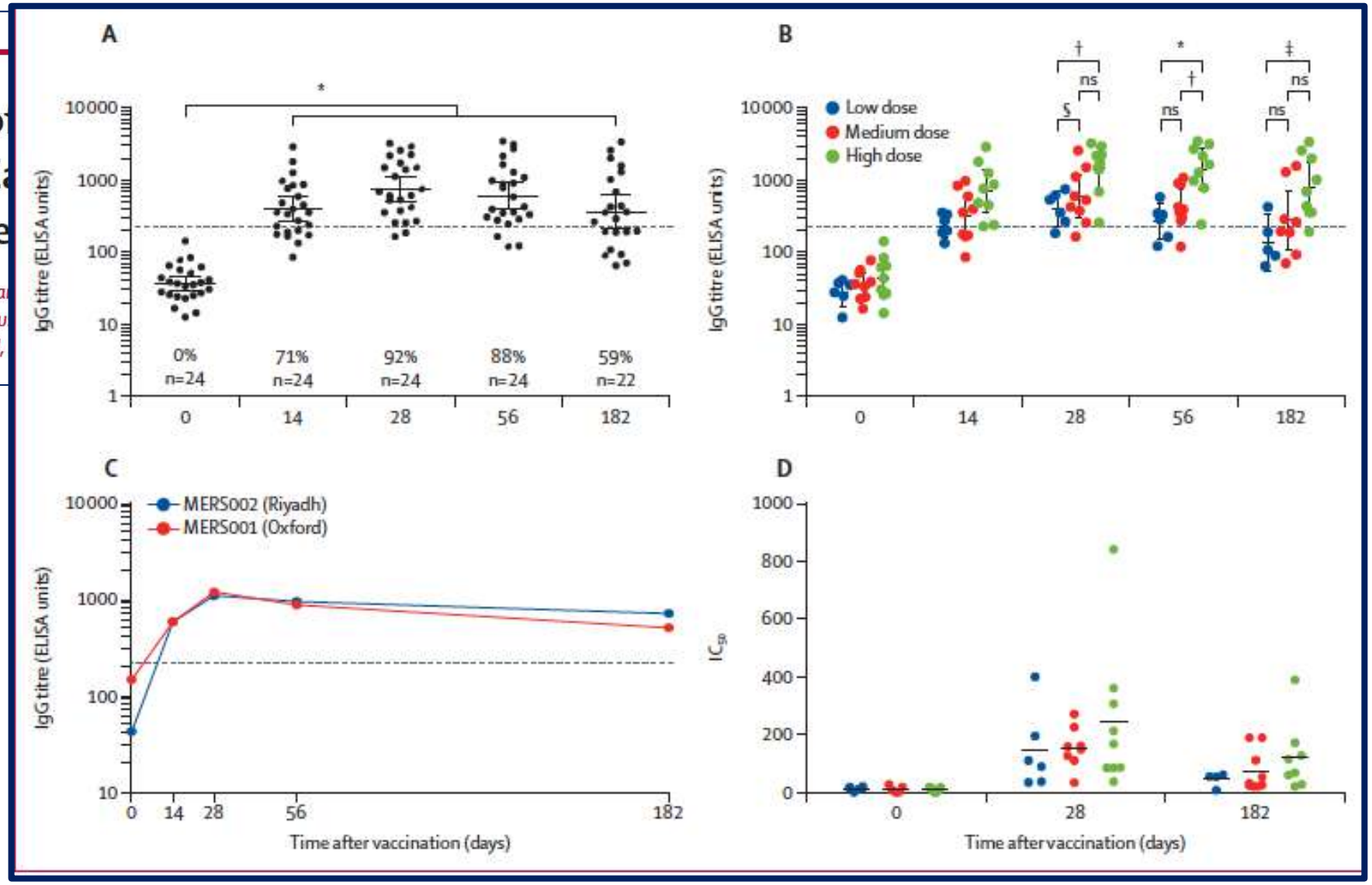
VİRAL VEKTÖR AŞILARI

MERS-CoV

Safety and immunogenicity of candidate in healthy Middle E an open-label, non-randomise

Mohammad Bosaeed, Hanan H Balkhy, Sultan Almaziad, Haya A Alja Mohammed W Alenazi, Abdulrahman Almasoud, Rawan Alanazi, Mu Pedro Folegatti, Fernando Ramos Lopez, Katie Ewer, Khalid Almoaikel,



Lancet Microbe 2022; 3: e11–20

ener çağrı dinleyici

VİRAL VEKTÖR AŞILARI

RSV

O060 / #506

CHAD155-VECTORED RESPIRATORY SYNCYTIAL VIRUS (RSV) INVESTIGATIONAL VACCINE (CHAD155-RSV) IS IMMUNOGENIC WHEN ADMINISTERED AT DIFFERENT DOSE LEVELS IN INFANTS AGED 6–7 MONTHS

PARALLEL SESSION
PRE-RECORDED +LIVE: ORAL PRESENTATIONS 07: RSV CLINICAL AND VACCINES

Evan Anderson[1], Fernando Baquero Artigao[2], Francois D Boucher[3], James Daniel Campbell[4], Guido Castelli Gattinara[5], Benhur Sirvan Cetin[6], Javier Díez-Domingo[7], Ener Cagri Dinleyici[8], Cristina Epalza[9], Saul Faust[10], Tolga Ince[11], Aleksander Krasnow[12], Ernest Kuchar[13], Joanne M Langley[14], Kathia Luciani[15], Mercedes Macias Parra[16], Miguel Angel Marin Gabriel[17], Federico Martinón-Torres[18], Jose Manuel Merino Arribas[19], Marisa Márcia Mussi-Pinhata[20], Ximena Norero[21], Jorge Pinto[22], Xavier Sáez-Llorens[21,23], Ignacio Salamanca De La Cueva[24], Leszek Szenborn[25], Henryk Szymanski[26], Bruce Tapiero[27], Ilkka Seppa[28], Eduardo López-Medina[29], Mika Rämet[28], Jose Tomas Ramos Amador[30], Thanyawee Puthanakit[31], Ilse Dieussaert[32], Damien Friel[33], Antonio Gonzalez Lopez[32,34], Roderick Mcphee[32,35], Vanja Nikic[32], Sonia K Stoszek[32], Wayne Woo[32,36], Nicolas Vanhoutte[37]

ener çağrı dinleyici

VİRAL VEKTÖR AŞILARI

RSV

Methods: In this phase I/II observer-blind, controlled study conducted in 13 countries, infants aged 6-7 months were randomized (1:1:1) to receive either 1 dose of ChAd155-RSV $1.5x10^{10}$viral particles (vp) and 1 placebo dose (RSV_1D group), 2 doses of ChAd155-RSV $5x10^{10}$vp (RSV_2D group) or 2 comparator doses (placebo or vaccine [meningococcal or pneumococcal]) on days 1 and 31. We evaluated RSV-A neutralizing antibody (NAb) geometric mean titers (GMTs; ED60) and anti-RSV F IgG geometric mean antibody concentrations (GMCs; EU/mL). We present results from RSV unexposed infants (seronaïve) as assessed by serologic testing of RSV-A NAbs at baseline.

Results: Of 201 infants enrolled, 155 were seronaïve and analyzed for immunogenicity up to day 61. At days 31 and 61, RSV-A NAb GMTs were significantly higher in RSV groups compared to baseline and comparator group (Figure A). The high dose vaccine (RSV_2D) induced greater RSV-A NAbs response as compared to low dose (RSV_1D) from baseline to day 31 (4.4-fold vs 2.9-fold increase, respectively). The second RSV vaccine dose (RSV_2D) induced a further increase of >2.6-fold in RSV-A NAb GMTs at day 61. In total, an 11.8-fold increase from baseline (GMT:21.2) to day 61 (GMT:246.0) was observed. Anti-RSV-F IgG followed similar trends, with increases at day 61 of 32.9-fold (GMC:2300.0; RSV_1D) and 150.0-fold (GMC:9082.3; RSV_2D) (Figure B).

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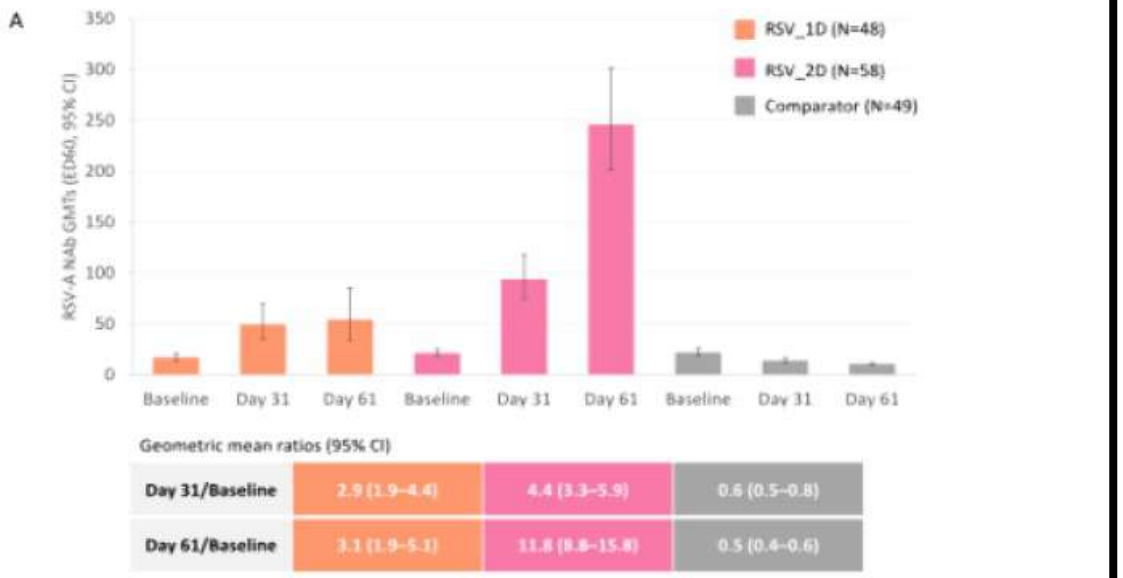
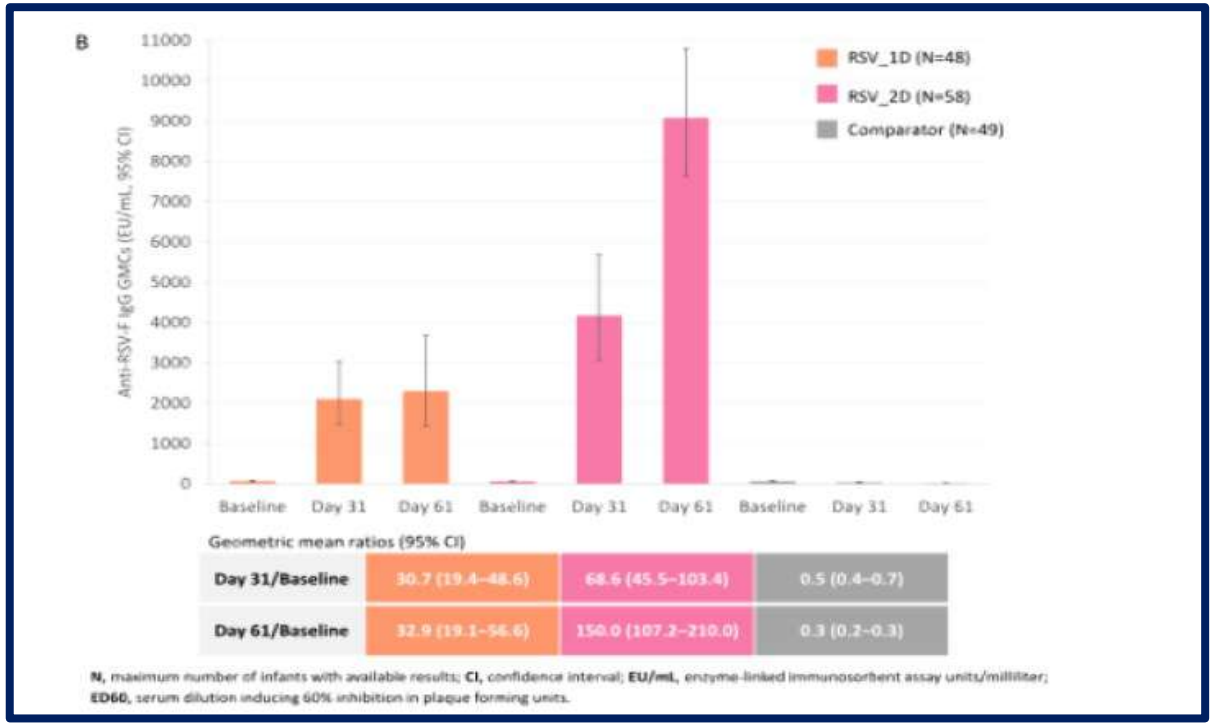
RSV

Figure. A. RSV-A NAb titers and B. Anti-RSV F IgG antibody concentrations of ChAd155-RSV dose levels until day 61 post-vaccination (seronaïve infants, per protocol set for immunogenicity)



Geometric mean ratios (95% CI)

Day 31/Baseline	2.9 (1.9–4.4)	4.4 (3.3–5.9)	0.6 (0.5–0.8)
Day 61/Baseline	3.1 (1.9–5.1)	11.8 (8.8–15.8)	0.5 (0.4–0.6)



Geometric mean ratios (95% CI)

Day 31/Baseline	30.7 (19.4–48.6)	68.6 (45.5–103.4)	0.5 (0.4–0.7)
Day 61/Baseline	32.9 (19.1–56.6)	150.0 (107.2–210.0)	0.3 (0.2–0.3)

N, maximum number of infants with available results; **CI**, confidence interval; **EU/mL**, enzyme-linked immunosorbent assay units/milliliter; **ED60**, serum dilution inducing 60% inhibition in plaque forming units.

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VİRAL VEKTÖR AŞILARI

RSV

REACTOGENICITY AND SAFETY OF CHAD155-VECTORED RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINE (CHAD155-RSV) ADMINISTERED AT DIFFERENT DOSE LEVELS IN INFANTS AGED 6–7 MONTHS

E-POSTER VIEWING
E-POSTER DISCUSSION SESSION 03: VACCINES 1

Evan Anderson[1], Fernando Baquero Artigao[2], Francois D Boucher[3], James Daniel Campbell[4], Guido Castelli Gattinara[5], Benhur Sirvan Cetin[6], Javier Díez-Domingo[7], Ener Cagri Dinleyici[8], Saul Faust[9], Tolga Ince[10], Aleksander Krasnow[11], Ernest Kuchar[12], Joanne M Langley[13], Kathia Luciani[14], Mercedes Macias Parra[15], Miguel Angel Marin Gabriel[16], Federico Martinón-Torres[17], Jose Manuel Merino Arribas[18], Marisa Márcia Mussi-Pinhata[19], Ximena Norero[20], Jorge Pinto[21], Xavier Sáez-Llorens[20,22], Ignacio Salamanca De La Cueva[23], Leszek Szenborn[24], Henryk Szymanski[25], Pablo Rojo Conejo[26], Bruce Tapiero[27], Ilkka Seppa[28], Eduardo López-Medina[29], Mika Rämet[28], Jose Tomas Ramos Amador[30], Thanyawee Puthanakit[31], Ilse Dieussaert[32], Damien Friel[33], Antonio Gonzalez Lopez[32,34], Roderick Mcphee[32,35], Vanja Nikic[32], Sonia K Stoszek[32], Wayne Woo[32,36], Nicolas Vanhoutte[37]

Results: Most frequently reported solicited local AEs (per infant) in RSV groups were pain (16.9-20.0%) and erythema (13.8-15.5%), but were reported generally less than after the control vaccine (42.9% and 61.9%, respectively). Solicited systemic AEs were reported in similar proportions across groups, with irritability/fussiness being the most frequent (40.9-64.3%). Fever (≥38.0°C) per dose in RSV groups (9.5-39.4%, 95% confidence interval [CI]:28.0-51.7%) appeared slightly higher than in the comparator groups (0.0-31.0%, 95% CI:17.6-47.1%) however, CIs overlap. Across all groups, 61.5-77.3% of infants experienced ≥1 unsolicited AE with comparable rates, grade and medical attendance (27.9-72.7%). SAEs reported until day 61 appear similar across groups. No safety concerns were found regarding potential ERD in the investigational groups.
Conclusions: Overall, no safety concern was detected with any ChAd155-RSV dose level/schedule.

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Times are changing

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KANSER AŞILARI

European Journal of Cancer 160 (2022) 150–174

Available online at www.sciencedirect.com

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journal homepage: www.ejcancer.com

Review

Therapeutic vaccines for breast cancer: Has the time finally come?

Chiara Corti [a,b], Pier P.M.B. Giachetti [a,b], Alexander M.M. Eggermont [c,d], Suzette Delaloge [d], Giuseppe Curigliano [a,b,*]

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Corti et al. European Journal of Cancer 2022

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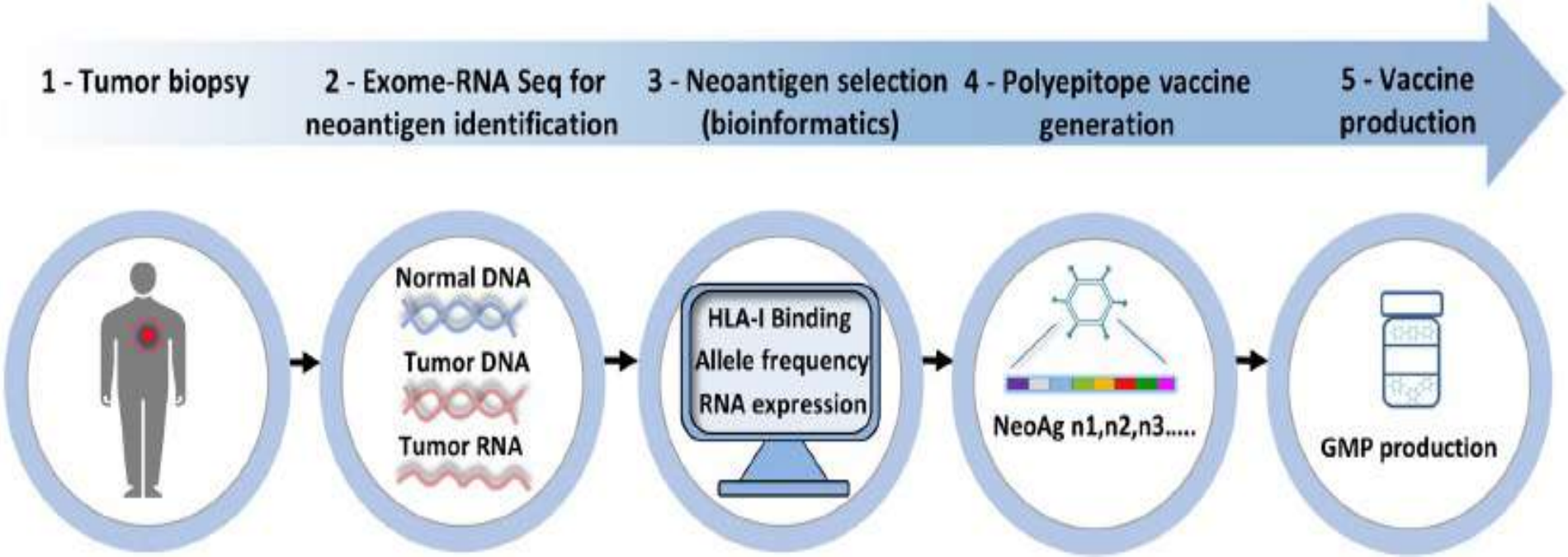

Fig. 3. Overview of the process for generation of patient-specific NHPAd based neoantigen cancer vaccine. 1. The Patient has the tumor biopsy taken. 2. Tumor DNA and RNA and healthy tissue DNA (e.g., PBMC) are sequenced in order to identify the tumor specific mutations by comparing the sequences from normal versus tumor DNA. 3. A prioritization strategy is utilized to select the best neoAg for inclusion into the vaccine, based on 3 parameters: predicted HLA-I binding, allele frequency, mRNA expression. 4. The selected neoAgs are joined head to tail, with the mutated amino acid (aa), determined by a one to three nucleotides mutation, at the center and flanked upstream and downstream by 12 wild-type aa, for a total length of 25aa for each neoAg. The corresponding gene is cloned in a NHPAd vector. 5. The vaccine is produced by a rapid (few weeks) GMP manufacturing process.

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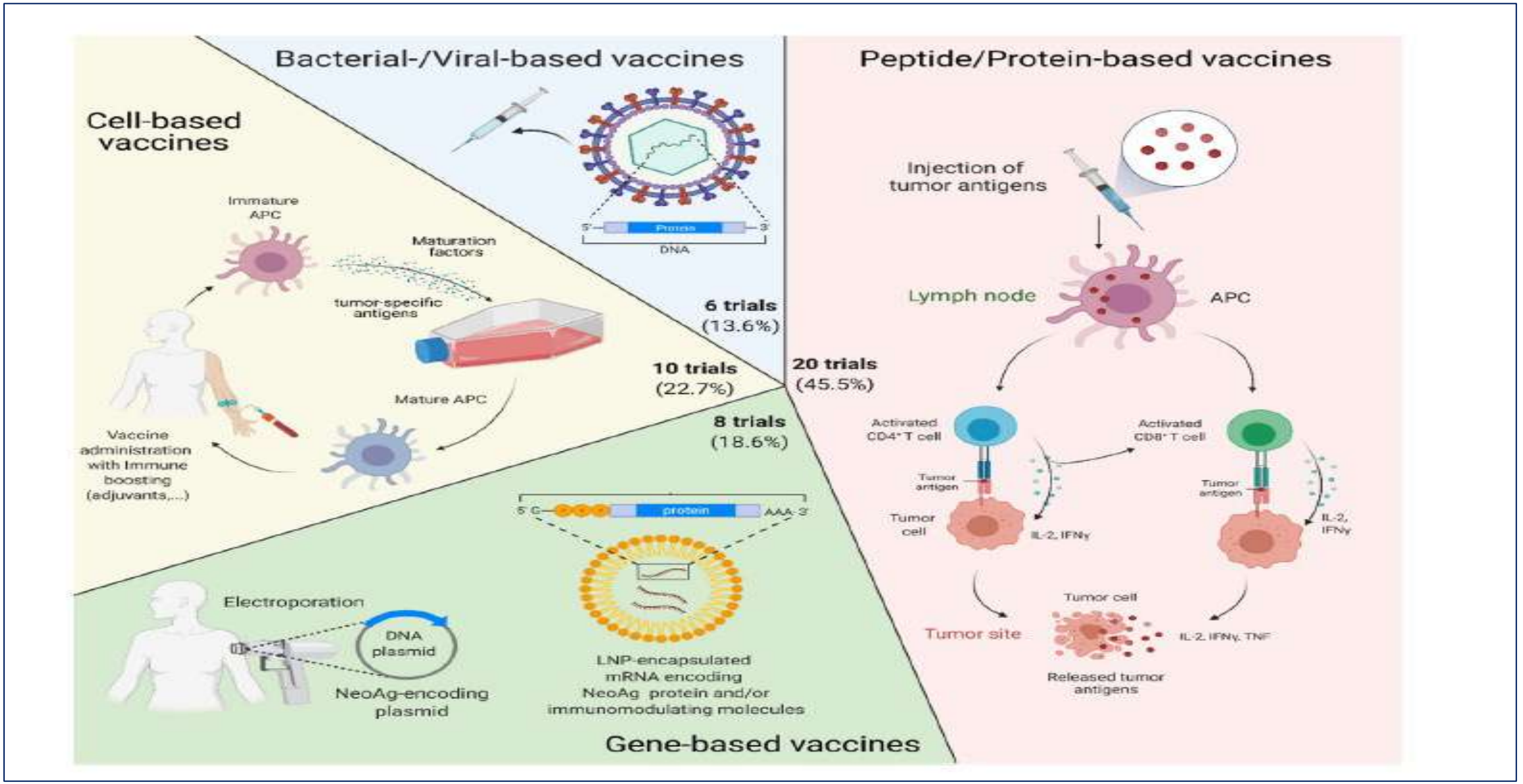
KANSER AŞILARI



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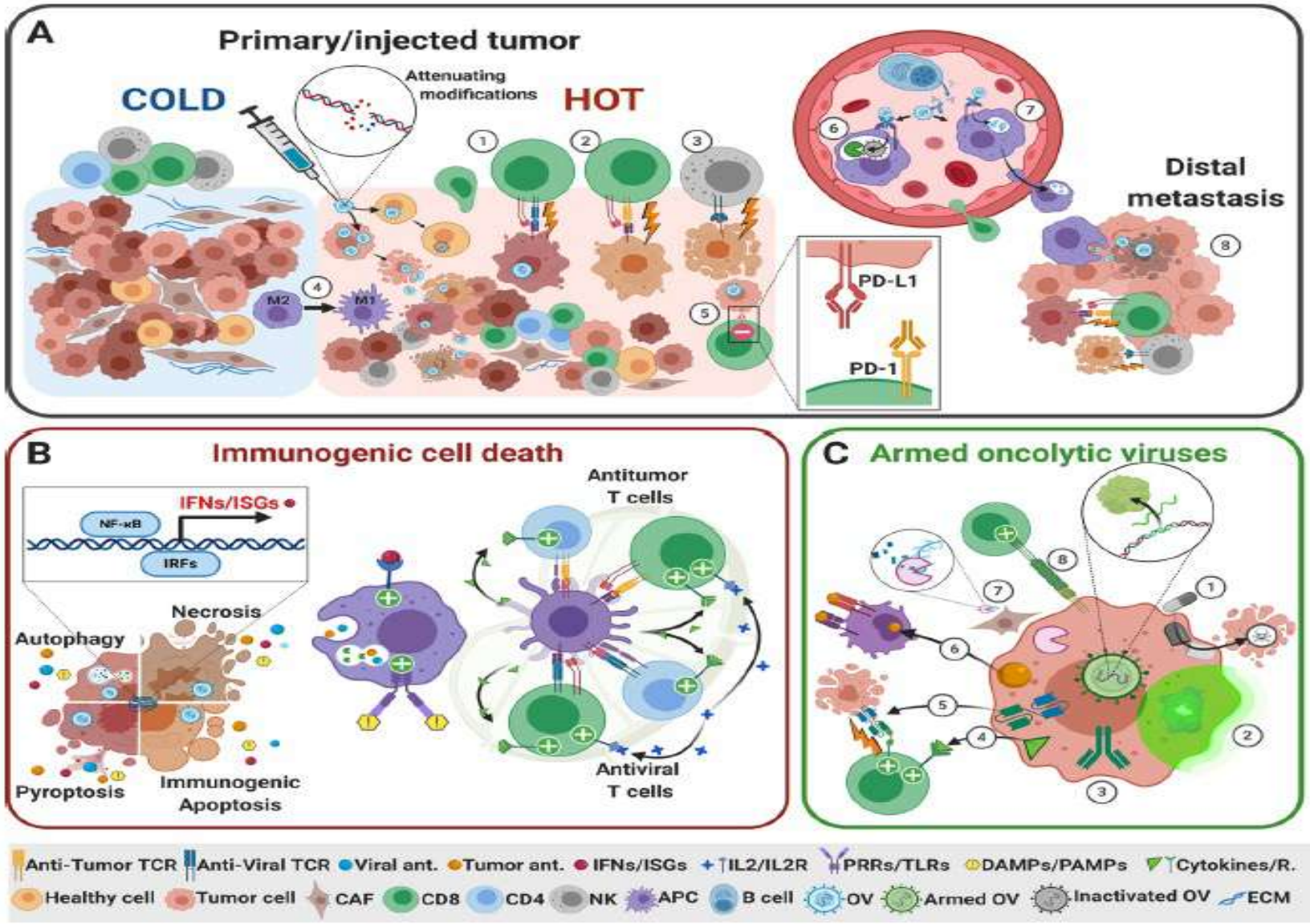

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AŞILAMA: EŞİT VE ADİL DAĞITIM

NEWS → NEWS STORIES → GPEI STATEMENT ON WPV1 IN MALAWI

17/02/2022

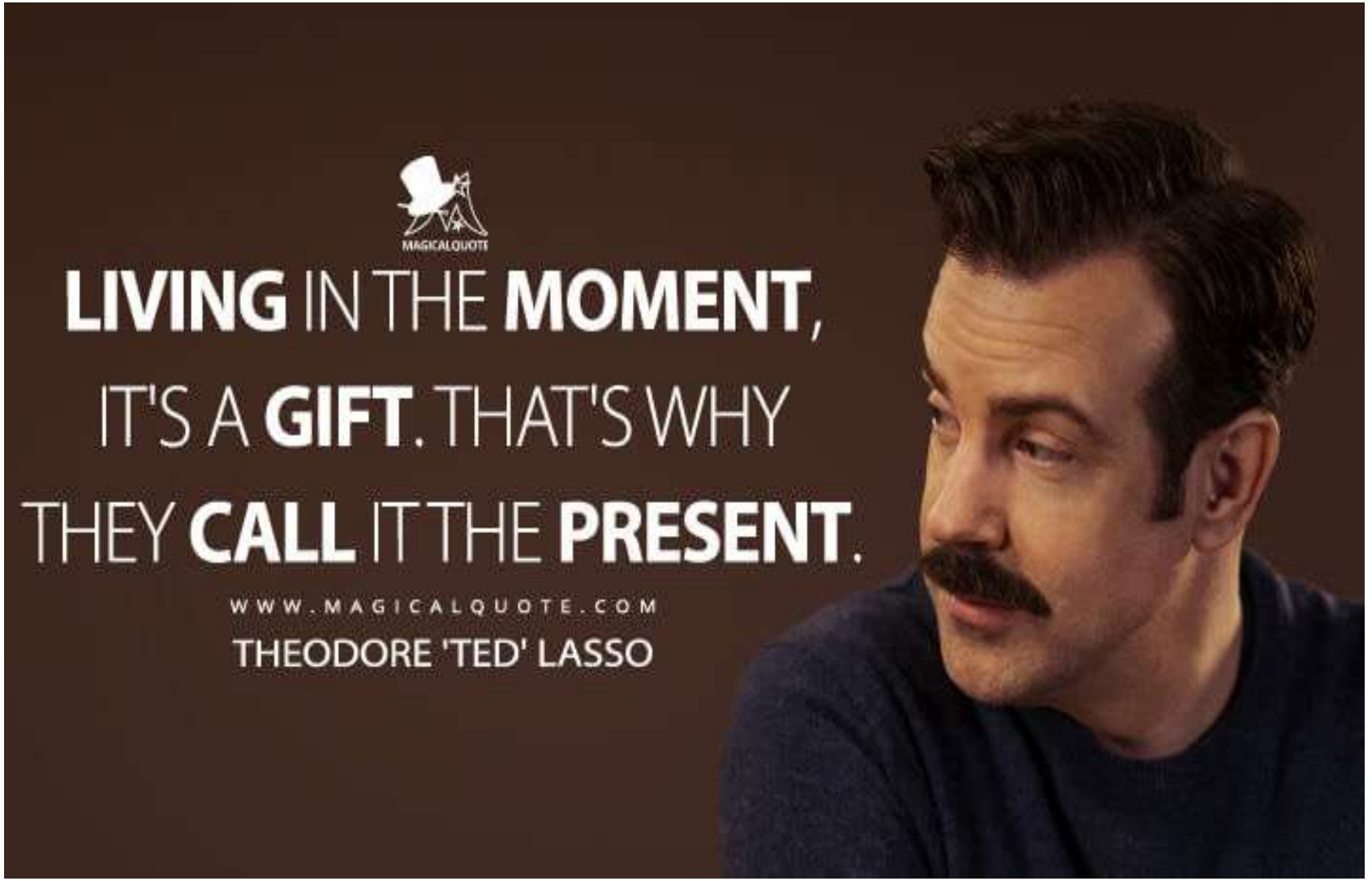
At-risk countries, Eradication, GPEI partners, Surveillance

GPEI Statement on WPV1 in Malawi

Wild poliovirus type 1 detected in Lilongwe, Malawi

17 February 2022 As a result of ongoing disease surveillance, the Global Polio Laboratory Network (GPLN) has confirmed the presence of type 1 wild poliovirus (WPV1) in a child suffering from paralysis in Tsabango, Lilongwe, Malawi. Analysis shows that the virus is genetically linked to WPV1 that was detected in Pakistan's Sindh province in October 2019.

The three-year-old girl in Malawi experienced onset of paralysis on 19 November 2021, and stool specimens were collected for testing on 26 and 27 November. Sequencing of the virus conducted in February by the National Institute for Communicable



Excellence is a road, not a destination

Cont'd, 2022. Ener Cagri Dinleyici