Leveraging Innovative Platforms for Novel Vaccines

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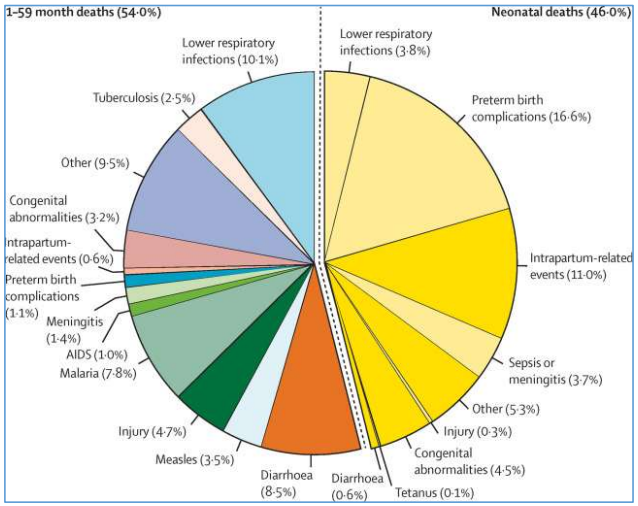
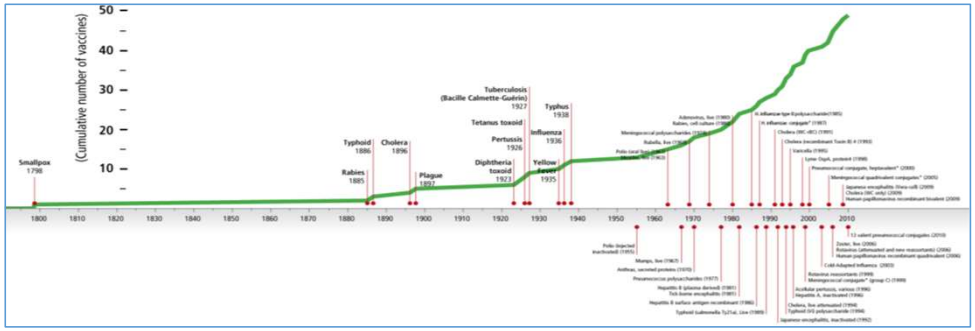
Successes & Challenges

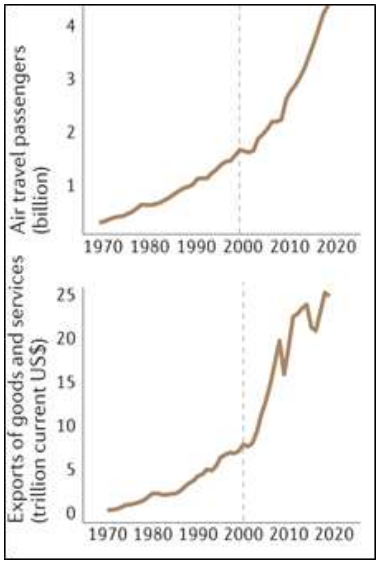
Over last century there has been development of numerous new vaccines both based on new platforms and for emerging diseases.





Lower vaccine coverage and unavailability of highly efficacious vaccines for some of the diseases the mortality rate remain high in under 5 year age group and especially in neonates.

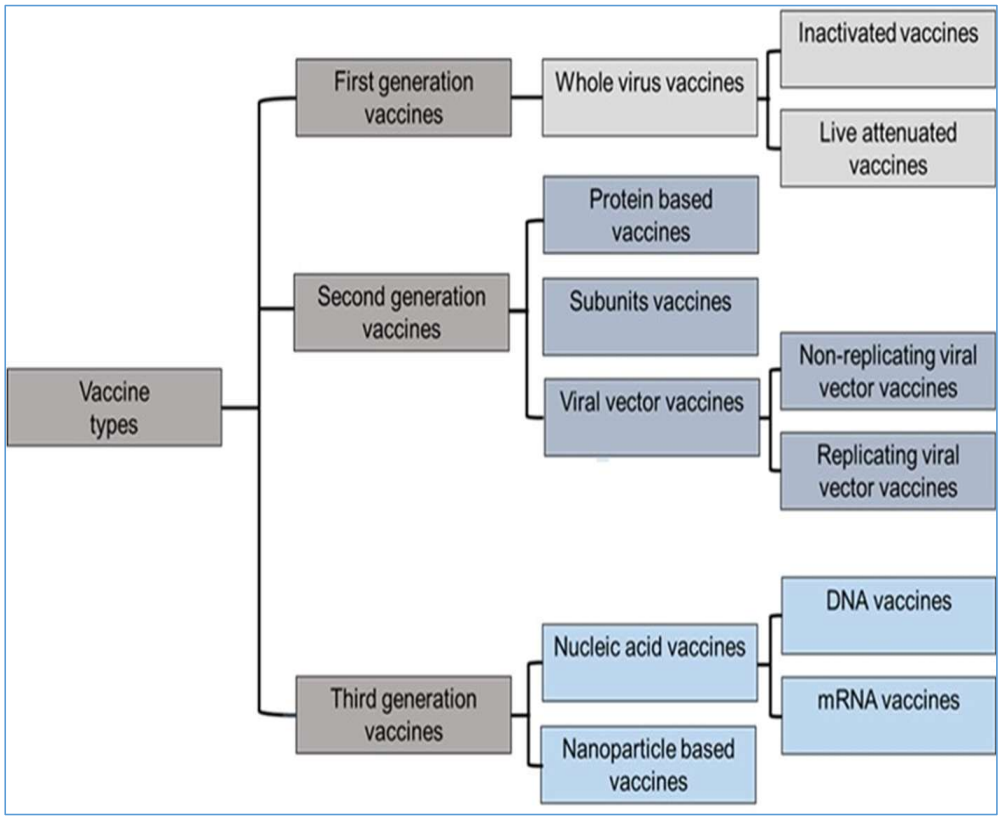
Climate Change has also led to emergence of new diseases and redistribution of existing diseases in various geographies. This is compounded by air travel, global exports and urbanization as disease can reach to pandemic proportions as seen in COVID-19.

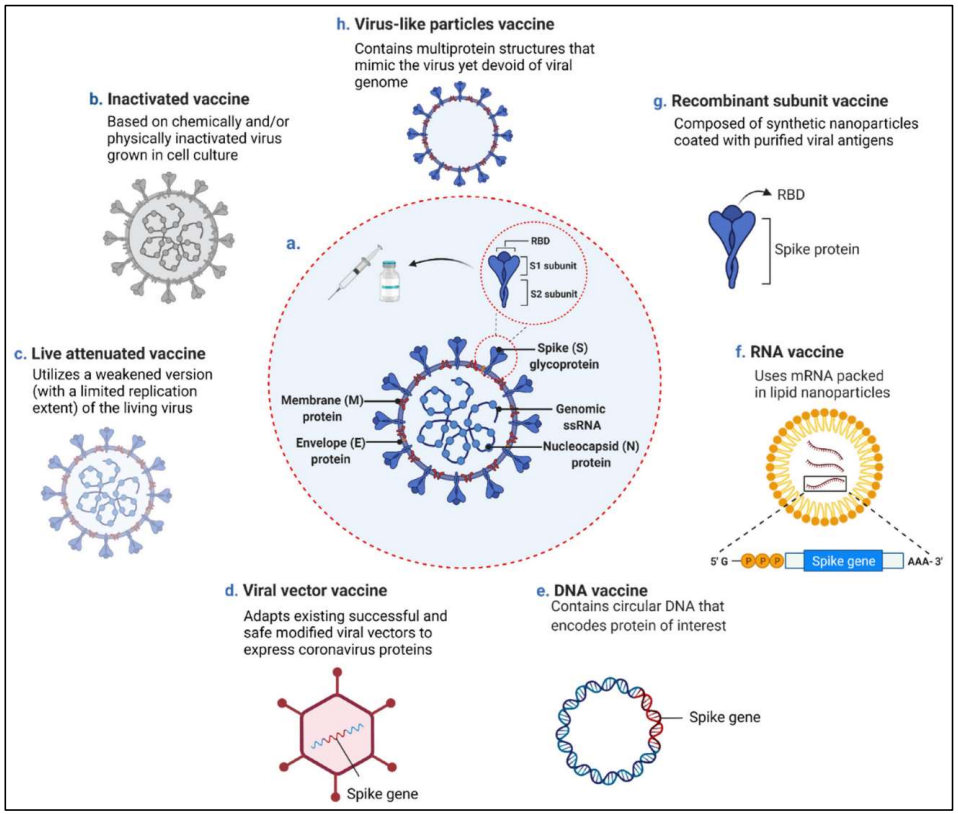


Year of first description	Name	Deaths
1918	'Spanish influenza'	In the range of about 50 million to 100 million
1931	Rift Valley Fever	Overall CFR < 1%; ~50% for hemorrhagic fever
1937	West Nile fever	CFR ~5%
1967	Marburg hemorrhagic fever	~470; very high CFR (24–88%, WHO)
1969	Lassa fever	~5,000 deaths annually; CFR 1–2%; Nigerian CFR 25%
1969	Acute hemorrhagic conjunctivitis	Rare
1976–2020	Ebola hemorrhagic fever	>15,000; CFR 75%
1981	HIV/AIDS	~37 million
1996	Avian flu	High CFR (60%)
1999	Nipah fever	<1,000; very high CFR
2002	SARS	813; CFR ~ 10%
2009	H1N1; H7N9 'swine flu'	284,000; CFR 2.9–9%
2012	MERS	935; CFR 34.4%
2014	Chikungunya	Rare
2015	Zika	Unknown
2019– 2023	COVID-19 (SARS-CoV-2)	>6.9 million; CFR 2–10%; high in elderly and individuals with comorbidities

Source: Plotkins
The Lancet Child & Adolescent Health, 6(2), 106-115, 2022
Nature Reviews Microbiology, 2022, 20: 193-205
Nature Medicine, 2021, 27: 591–600

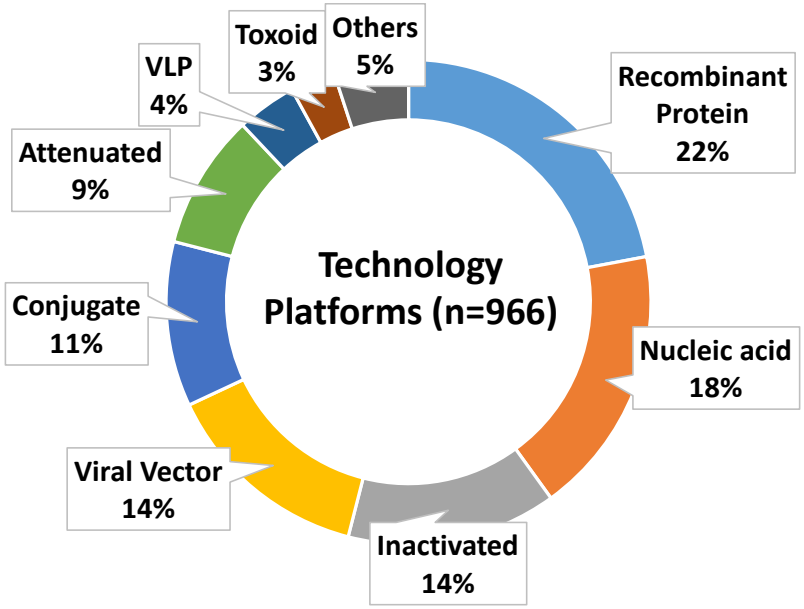
Platforms for vaccine development





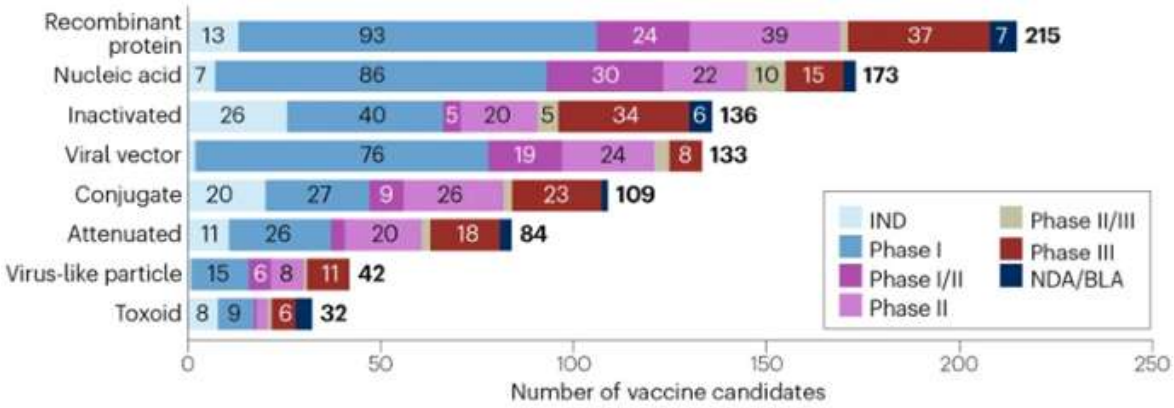
Source: Trop Dis Travel Med Vaccines, 2022, 8:20
Vaccines 2021, 9(10), 1196; https://doi.org/10.3390/vaccines9101196

Global Landscape of Vaccine Candidates in Development - 2023

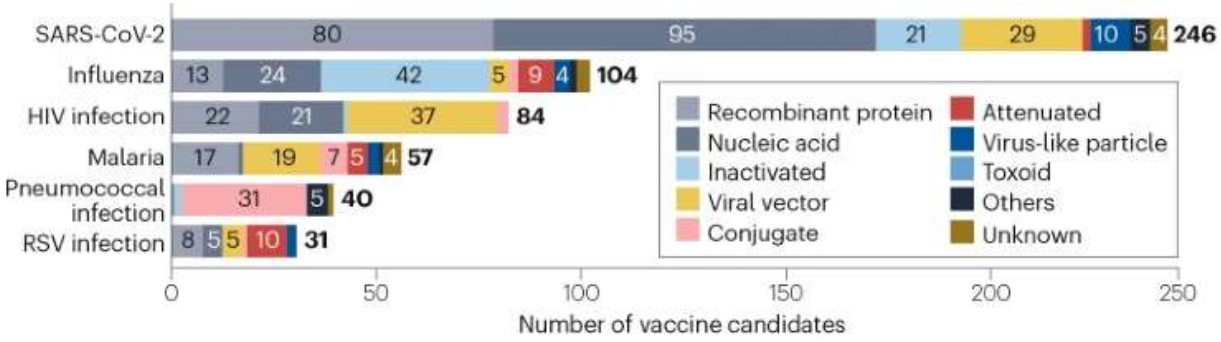


Only 23% candidate are based on traditional inactivated or attenuated vaccine platforms

Developmental Phase



Technology Platform in use for top six diseases

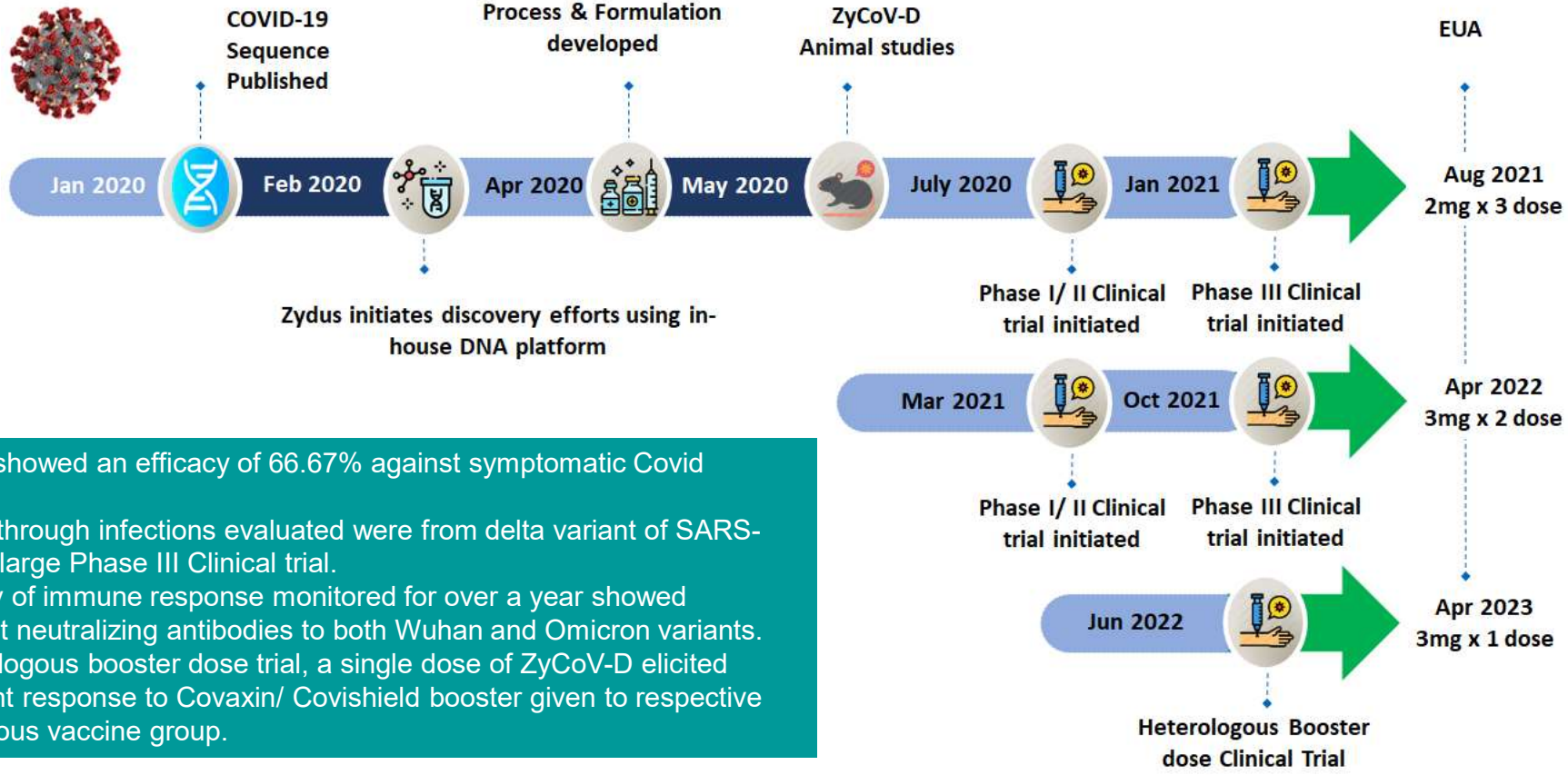


Source: Nature Review Drug Discovery, 2023. doi: 10.1038/d41573-023-00119-4. Epub ahead of print. PMID: 37474662.

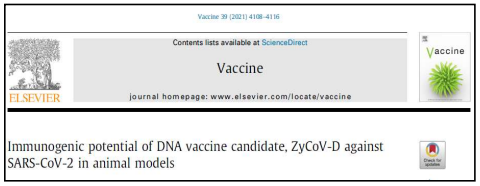
ZyCoV-D

World's First Human DNA based Vaccine

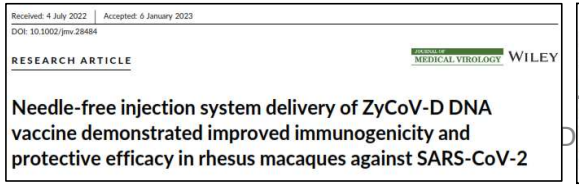
ZyCoV-D Vaccine Development



- Vaccine showed an efficacy of 66.67% against symptomatic Covid infection.
- All breakthrough infections evaluated were from delta variant of SARS-Cov-2 in large Phase III Clinical trial.
- Durability of immune response monitored for over a year showed persistent neutralizing antibodies to both Wuhan and Omicron variants.
- In heterologous booster dose trial, a single dose of ZyCoV-D elicited equivalent response to Covaxin/ Covishield booster given to respective homologous vaccine group.


Vaccine

Immunogenic potential of DNA vaccine candidate, ZyCoV-D against SARS-CoV-2 in animal models

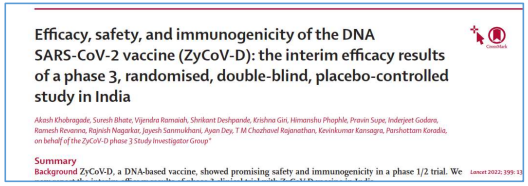

RESEARCH ARTICLE

Needle-free injection system delivery of ZyCoV-D DNA vaccine demonstrated improved immunogenicity and protective efficacy in rhesus macaques against SARS-CoV-2

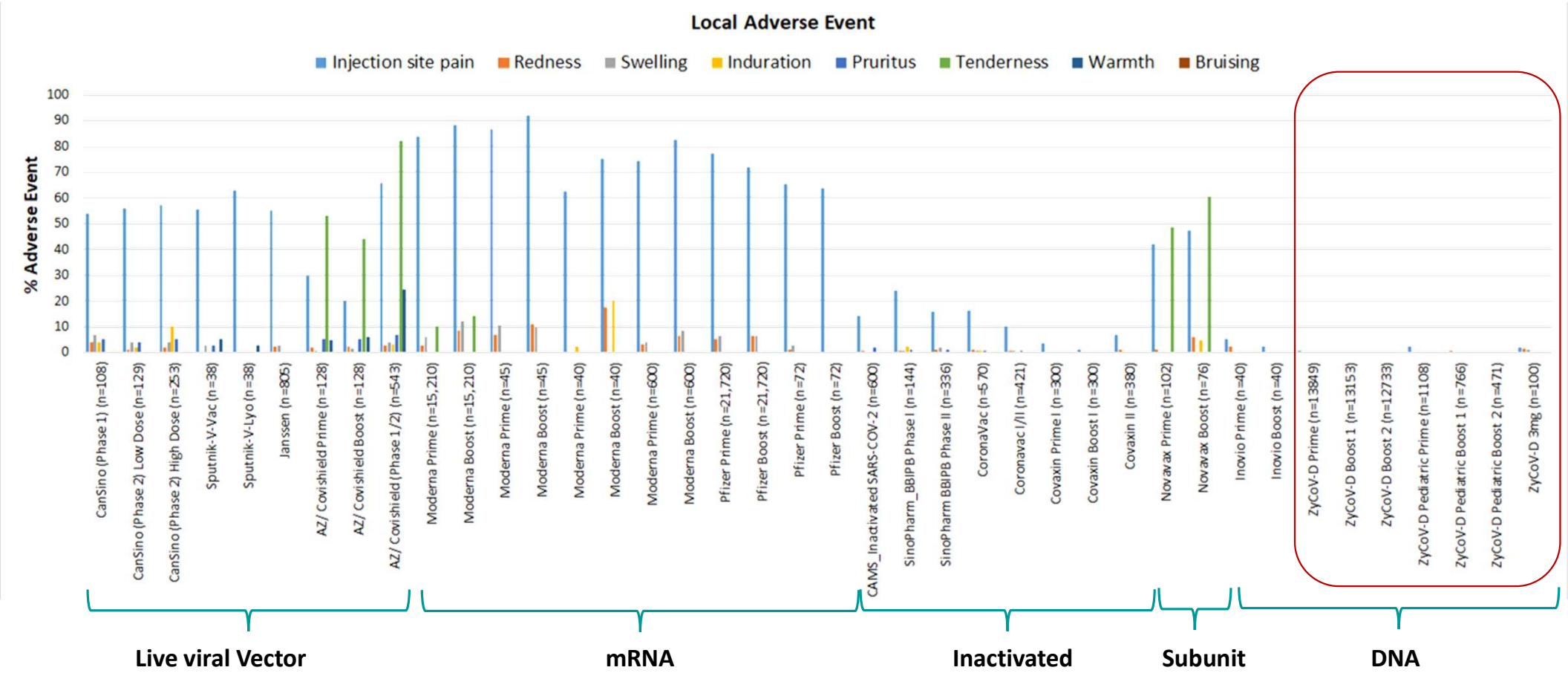

EClinicalMedicine

Research Paper

Safety and Immunogenicity of a DNA SARS-CoV-2 vaccine (ZyCoV-D): Results of an open-label, non-randomized phase I part of phase I/II clinical study by intradermal route in healthy subjects in India


Efficacy, safety, and immunogenicity of the DNA SARS-CoV-2 vaccine (ZyCoV-D): the interim efficacy results of a phase 3, randomised, double-blind, placebo-controlled study in India

Comparative Safety Profile of ZyCoV-D Vaccine as compared to other vaccines as per the published systematic review and meta-analysis



Adapted from: McDonald et al. Comparative systematic review and meta-analysis of reactogenicity, immunogenicity and efficacy of vaccines against SARS-CoV-2. NPJ Vaccines, 2021, 74:1

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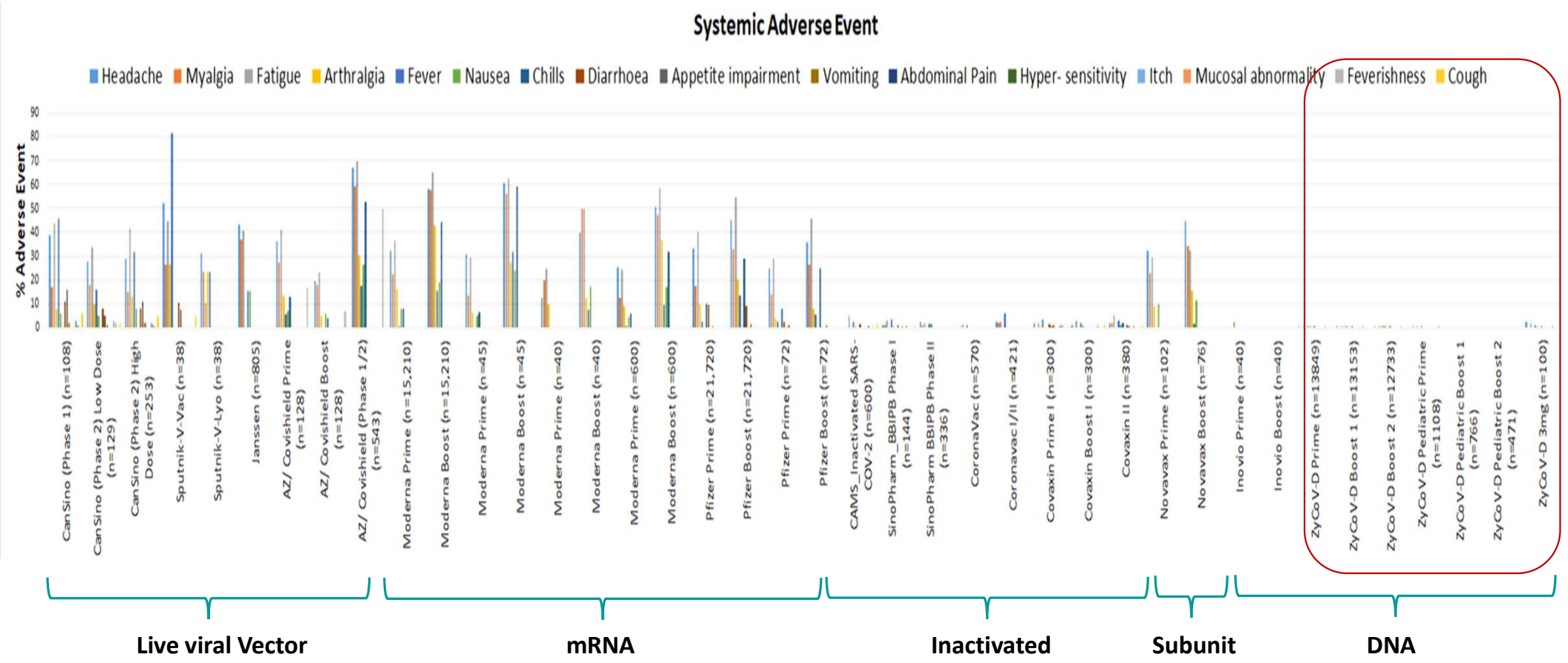

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Attributes of ZyCoV-D Vaccine

Safety Profile

- The **vector used** for development of ZyCoV-D is developed as per Food and Drug Administration (FDA) document, "Considerations for Plasmid DNA Vaccines for Infectious Disease Indications" and was demonstrated to be safe in several clinical trials
- **Preclinical Toxicity** - Repeat dose toxicity studies demonstrated vaccine to be safe and well tolerated even at 6mg dose in rats and 3mg dose in rabbits.
- **Bio-Distribution studies** in rats showed complete clearance of pDNA with couple of weeks post injection
- **Phase I Clinical Trial** – All volunteers were monitored for 24 hours in an ICU setting and subsequently for one week to evaluate complete safety profile. Vaccine was found to be safe and very well tolerated.
- **Anti-Nuclear Antibody (ANA)** Profiling of a subset of clinical samples showed no response.
- **Phase II and Phase III Clinical Trial** - Demonstrated Safety and Efficacy in over 28000 subjects for 2mg, 3 dose regimen and later in 3000 subjects for 3mg. 2 dose regimen.

Needle Free Delivery

- PharmaJet® delivery being **Needle-Free is useful in cases of "Trypanophobia"** (generally found in 1 of 4 adults) or in general for enhancing acceptance in children and adults
- This delivery system also **eliminates needle stick injuries** and reduces disease transmission risk due to use of contaminated needles (HIV, etc.)
- Needle free delivery will contribute **significantly in reduction of sharp waste management**

Stability

- ZyCoV-D is **stable at room temperature (25 deg. C) for couple of months** thus enabling distribution and handling in even the remotest regions of India.
- The vaccine also shows **no impact of multiple freeze thaw cycle** which is a major problem during vaccine transportation and leads to huge vaccine wastage globally.
- Vaccine is found to be **stable and usable for up to 14 days after opening as per open-vial study** which will significantly help in reducing the vaccine wastage

Plug & Play Technology

- **Easily adaptable technology wherein the antigen can be modified** or changed rapidly based on **new emerging variants** of the SARS-CoV-2 virus. This will provide flexibility in programmatic implementation to switch to newer vaccine candidates based on new variants (subject to regulatory approvals/ clearance) and thereby providing faster control of pandemic

Thank You