Viral Vector Delivery

Using Adeno5 to develop Inhalation Vaccine

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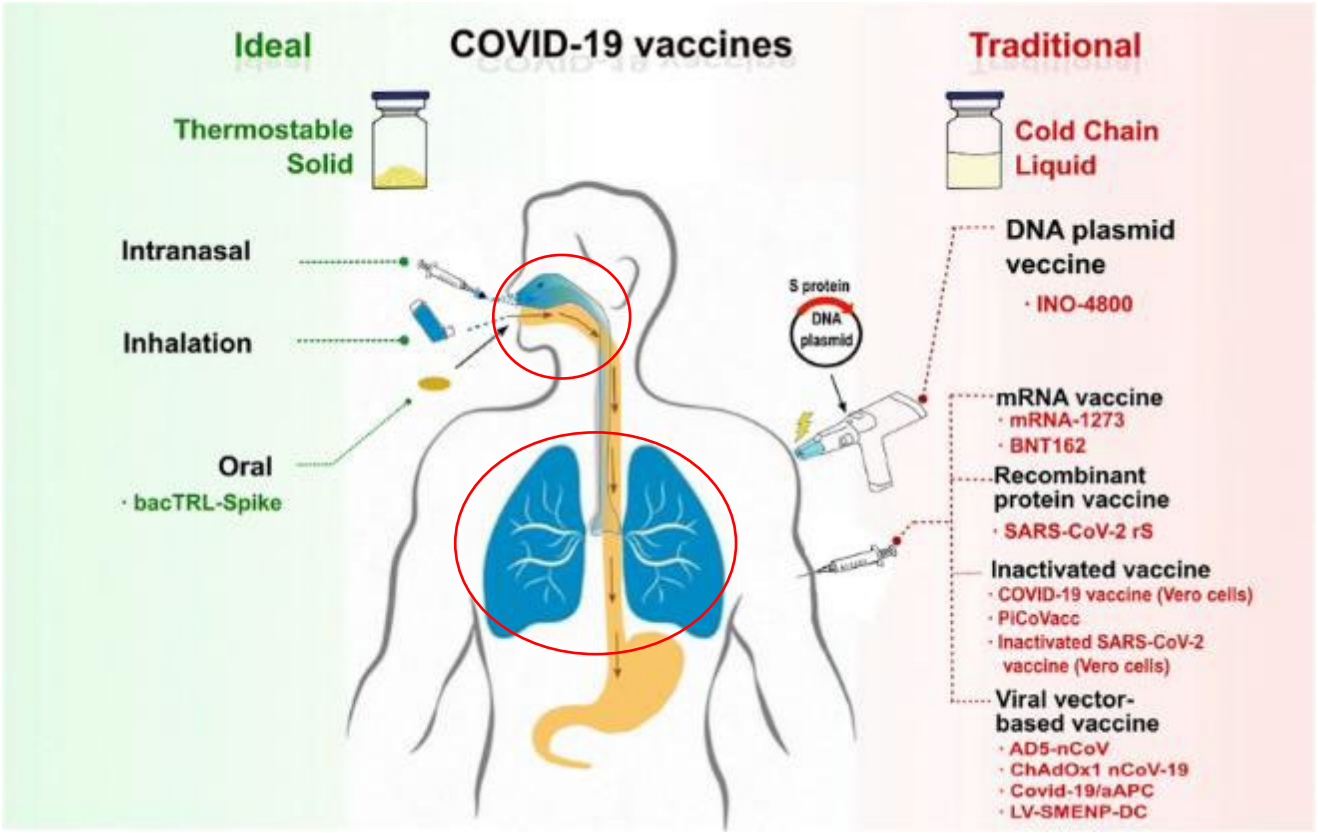
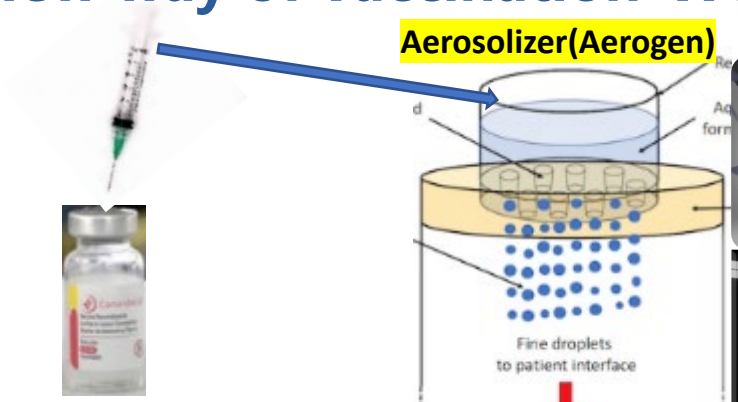
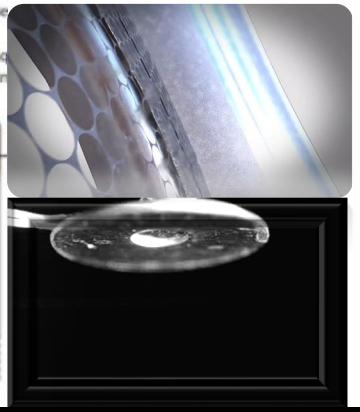
Current Vaccine are all muscle Injection to induce the system immune response but less protection at virus entry



New way of vaccination-World 1st Inhalation Vaccine





Directly using 0.1ml IM vaccine

1 cup=7 billion droplets

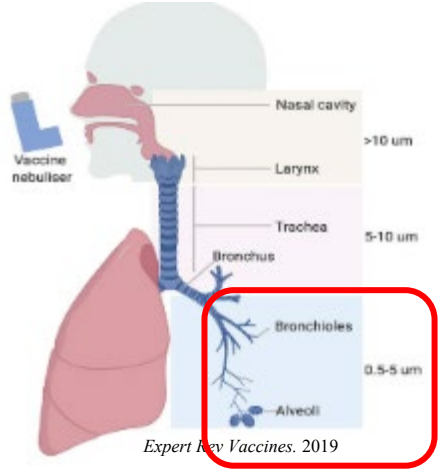
Humoral
Cellular
Mucosal

No Needle
No Pain
3 Layers Protection

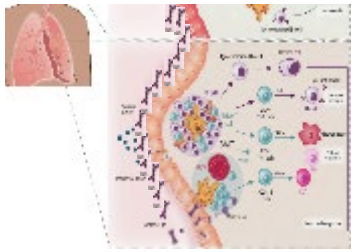
PEOPLE LOVE IT!

Characterization of Aerosolized Ad5-nCoV

Vaccine deposition following aerosol delivery



Expert Rev Vaccines. 2019

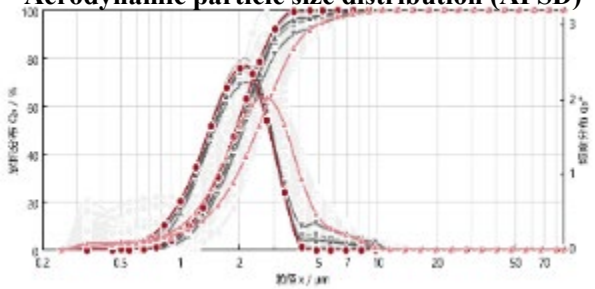


100 m2 surface area

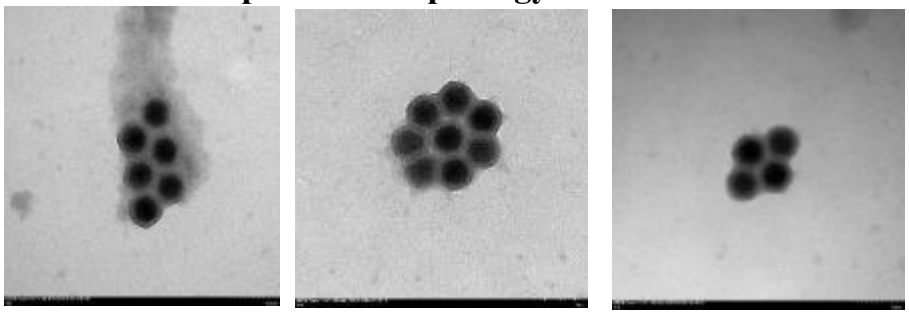
Viability of aerosolized vaccine

Dosage (ml)	Infections unit (IFU) recovery (%)	Viral particles (VP) recovery (%)
0.1	81.28%	97.54%
0.2	98.62%	96.45%

Aerodynamic particle size distribution (APSD)



No impact on morphology of Ad5-nCoV



Pre **Nebulize 0.1ml** **Nebulize 0.2ml**

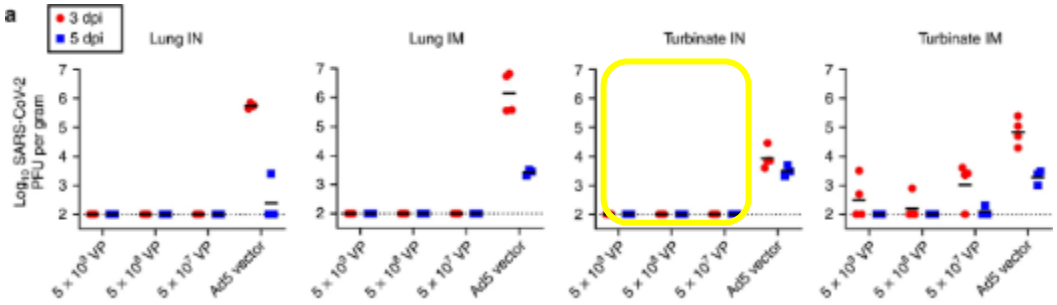
Mucosal Vaccination in Animal Models

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-020-17972-1 OPEN

A single dose of an adenovirus-vectored vaccine provides protection against SARS-CoV-2 challenge



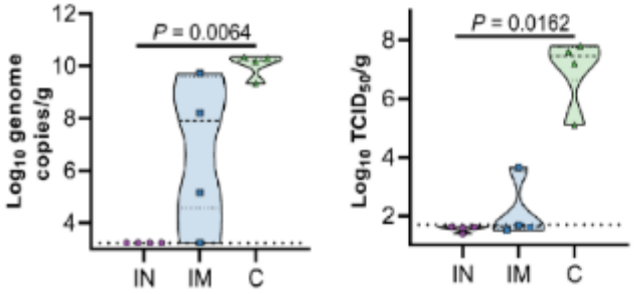
Complete protection for the upper and lower respiratory tracts against SARS-CoV-2 infection can be achieved using a single mucosal inoculation of Ad5-nCoV via IN route in mice.

Institute of Biotechnology & CanSinoBIO

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CORONAVIRUS

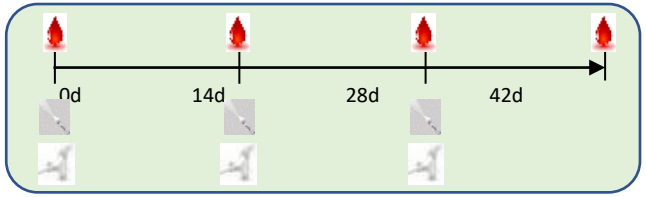
Intranasal ChAdOx1 nCoV-19/AZD1222 vaccination reduces viral shedding after SARS-CoV-2 D614G challenge in preclinical models

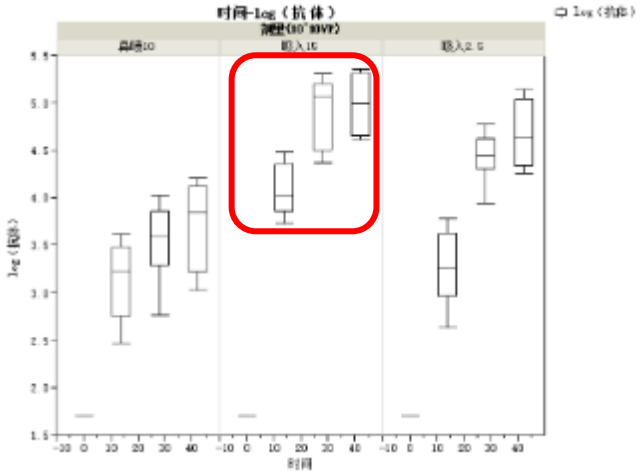


In both hamster and rhesus macaque models, intranasal vaccination with AZD1222 reduced viral shedding in upper and lower respiratory tracts.

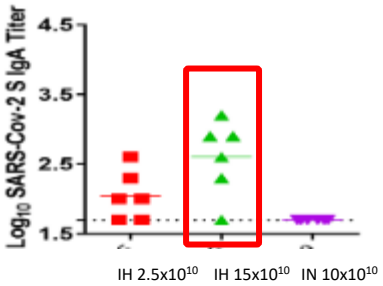
The University of Oxford

Which Is Better: Inhalation VS Intranasal?





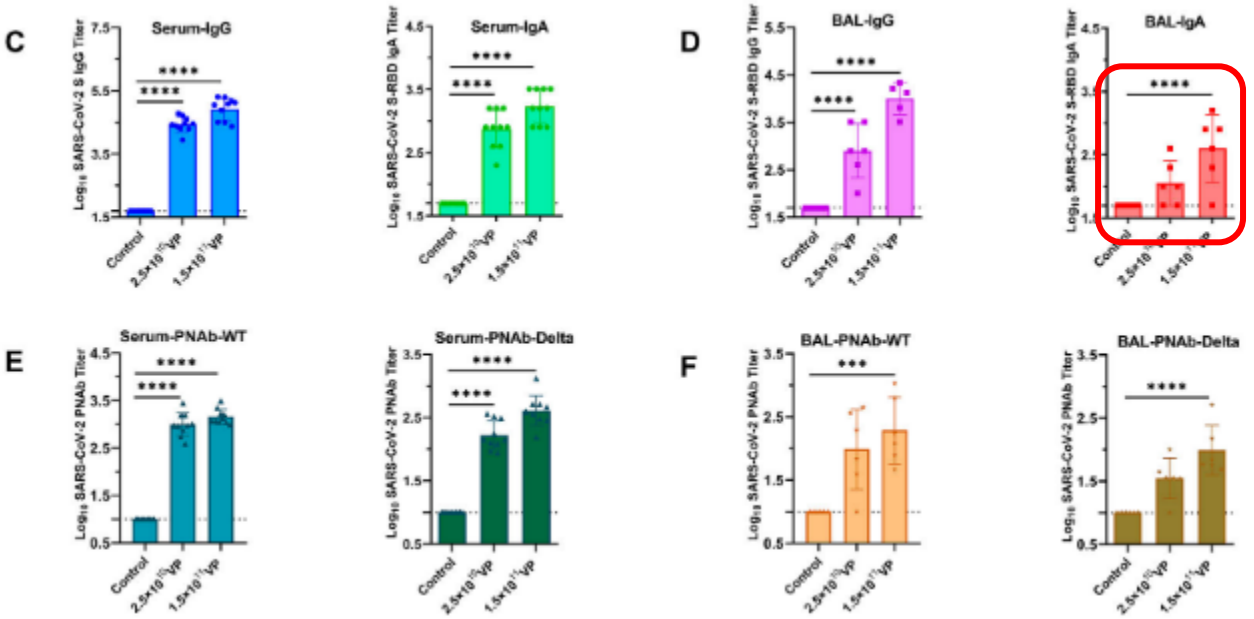
Group	Sample	Route ofa Administration	Dose (VP/L)	# of animal (NHP)
1	placebo	IH	0	10
2	Vaccine	IH	2.5×10^{10}	10
3	Vaccine	IH	15×10^{10}	10
4	Vaccine	IN	10×10^{10}	10



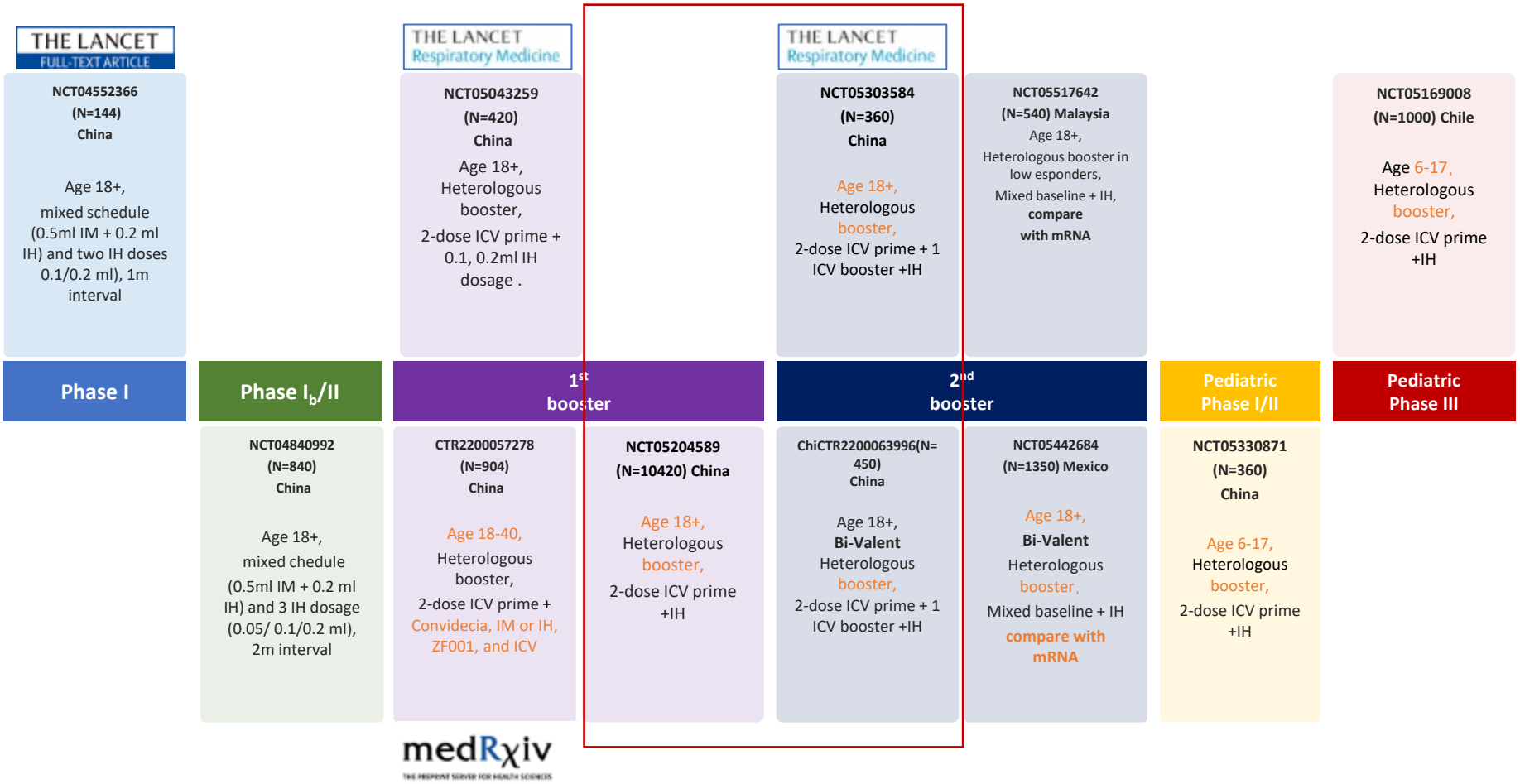
In rhesus monkey，with only ¼ dose as intranasal route，the IH group induced 10X antibodies against covid-19.

IH induced significant higher lever of sIgA (3dpi) than IN route in bronchoalveolar lavage(BAL).

Non-Clinical Studies – Immunogencitiy of Convidecia Air™ in Monkeys

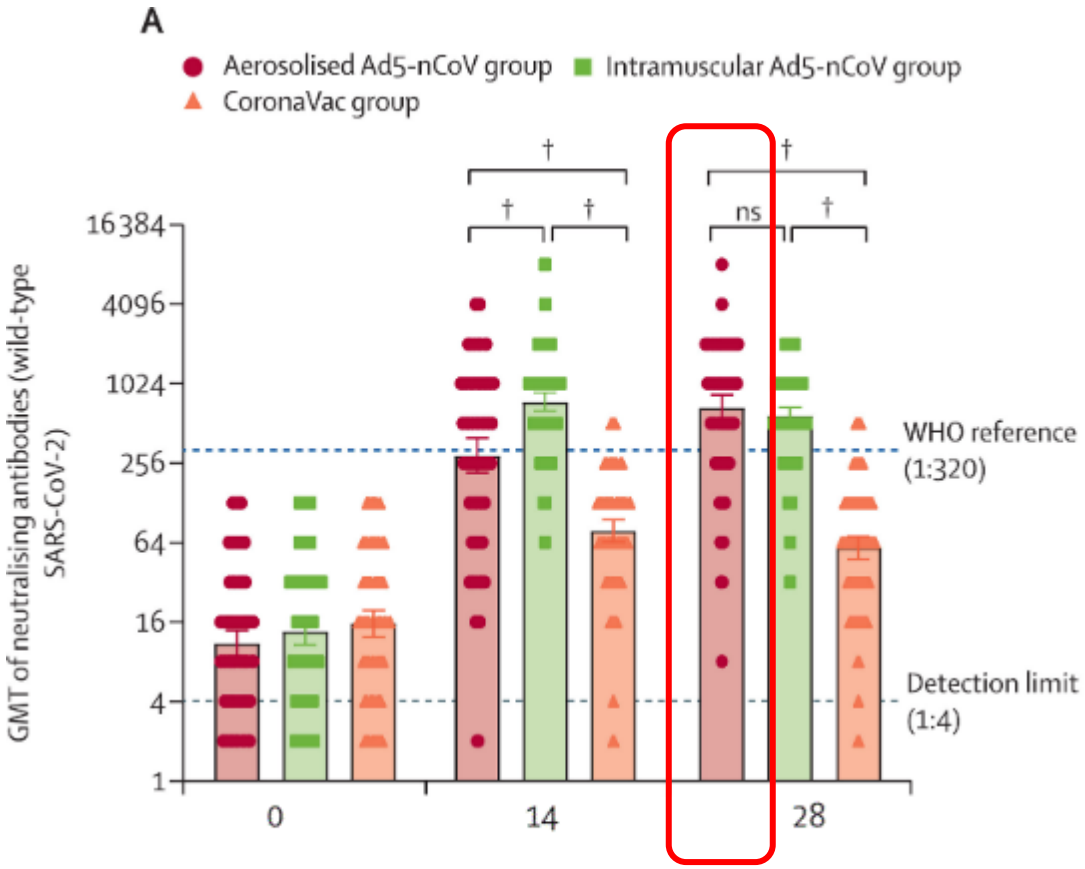


- (C and D) S-specific humoral immune responses in serum and bronchoalveolar lavage.
- (E and F) Pseudovirus neutralization antibody (PNAb) titres for SARS-CoV-2 WT or Delta variant were elevated in blood and **Bronchoalveolar lavage(BAL)**, respectively. ****P<0.0001, ***P<0.001.

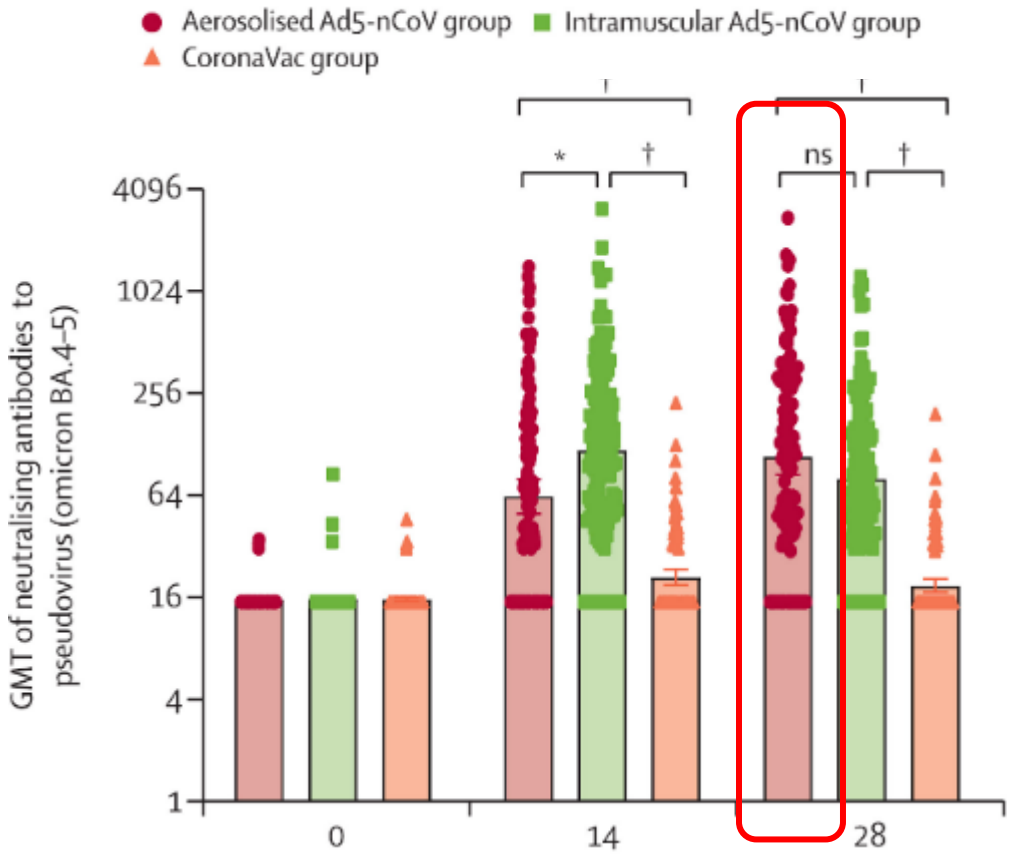

THE LANCET
FULL-TEXT ARTICLE
NCT04552366
(N=144)
China
Age 18+,
mixed schedule
(0.5ml IM + 0.2 ml IH) and two IH doses 0.1/0.2 ml), 1m interval
THE LANCET
Respiratory Medicine
NCT05043259
(N=420)
China
Age 18+,
Heterologous booster,
2-dose ICV prime + 0.1, 0.2ml IH dosage .
THE LANCET
Respiratory Medicine
NCT05303584
(N=360)
China
Age 18+,
Heterologous booster,
2-dose ICV prime + 1 ICV booster +IH
NCT05517642
(N=540) Malaysia
Age 18+,
Heterologous booster in low esponders,
Mixed baseline + IH,
compare with mRNA
NCT05169008
(N=1000) Chile
Age 6-17,
Heterologous booster,
2-dose ICV prime +IH
Phase I
Phase Ib/II
1st booster
2nd booster
Pediatric Phase I/II
Pediatric Phase III
NCT04840992
(N=840)
China
Age 18+,
mixed chedule
(0.5ml IM + 0.2 ml IH) and 3 IH dosage (0.05/ 0.1/0.2 ml), 2m interval
CTR2200057278
(N=904)
China
Age 18-40,
Heterologous booster,
2-dose ICV prime + Convidecia, IM or IH, ZF001, and ICV
NCT05204589
(N=10420) China
Age 18+,
Heterologous booster,
2-dose ICV prime +IH
ChiCTR2200063996(N=450)
China
Age 18+,
Bi-Valent
Heterologous booster,
2-dose ICV prime + 1 ICV booster +IH
NCT05442684
(N=1350) Mexico
Age 18+,
Bi-Valent
Heterologous booster,
Mixed baseline + IH
compare with mRNA
NCT05330871
(N=360)
China
Age 6-17,
Heterologous booster,
2-dose ICV prime +IH
medRxiv

Aerosolized Ad5-nCoV as 2nd Booster

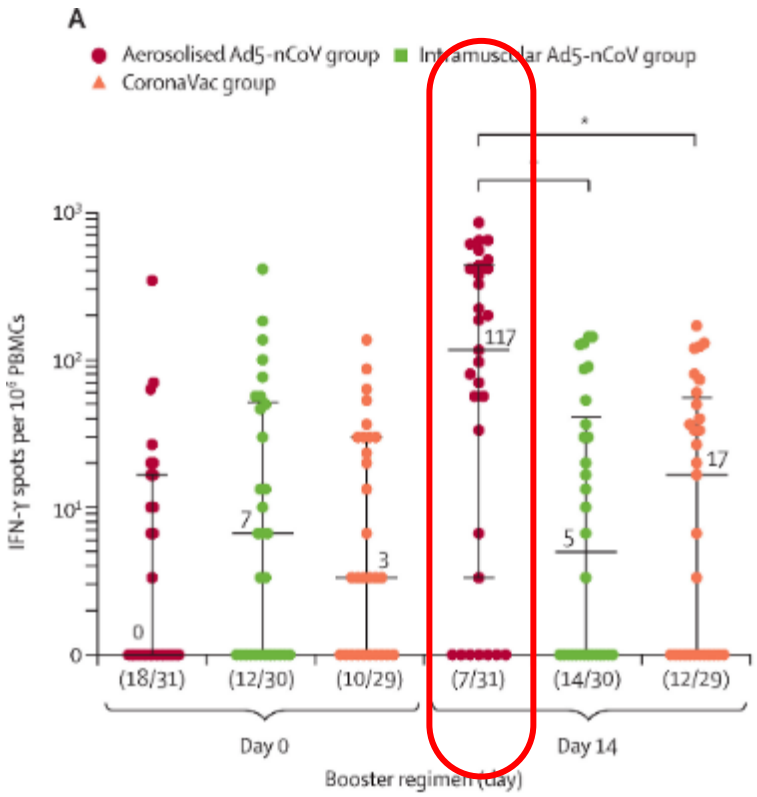
For the original strain, the levels of neutralizing antibodies in the aerosolized Ad5-nCoV group and the intramuscular injection of Ad5-nCoV group were significantly higher than those in the inactivation group



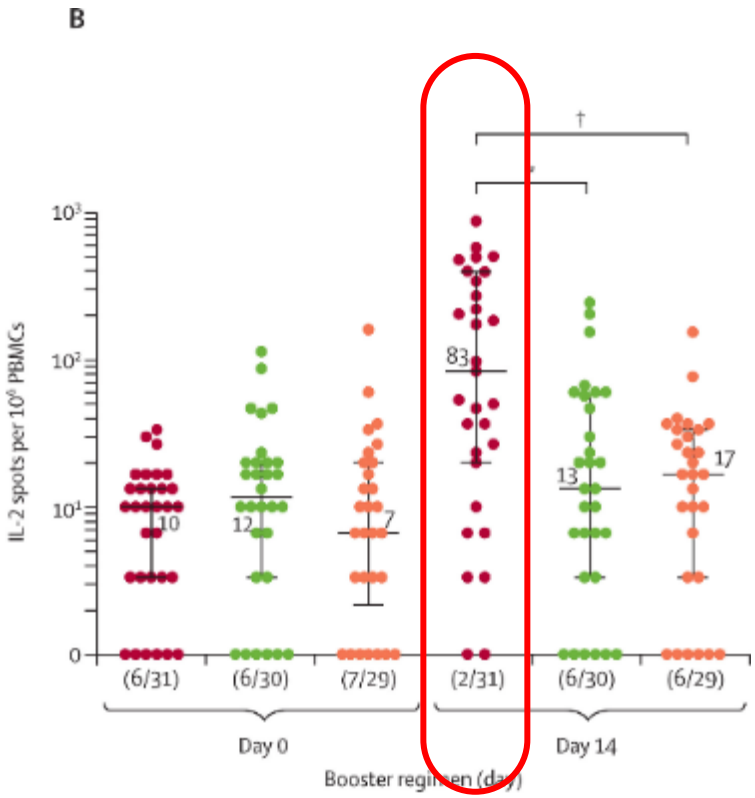
For Omicron BA.4/5, the levels of neutralizing antibodies in the aerosolized Ad5-nCoV group and the intramuscular injection of Ad5-nCoV group were significantly higher than those in the inactivation group



The aerosolized Ad5-nCoV group induced a significant cellular immune response

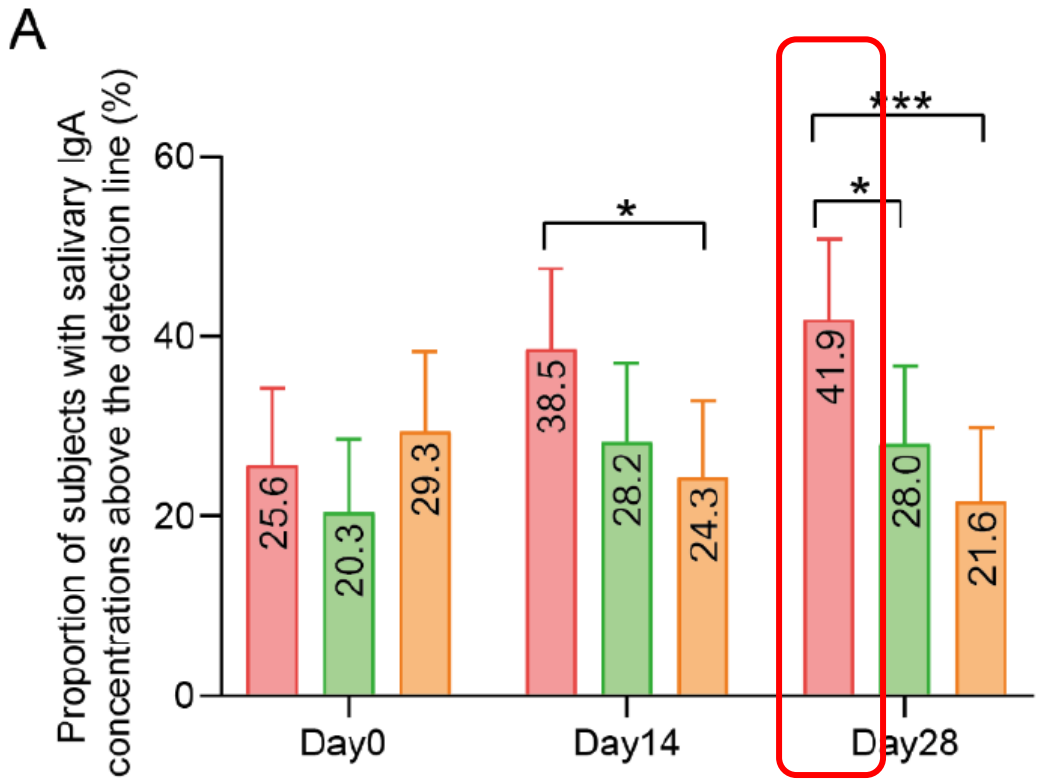


IFN-γ

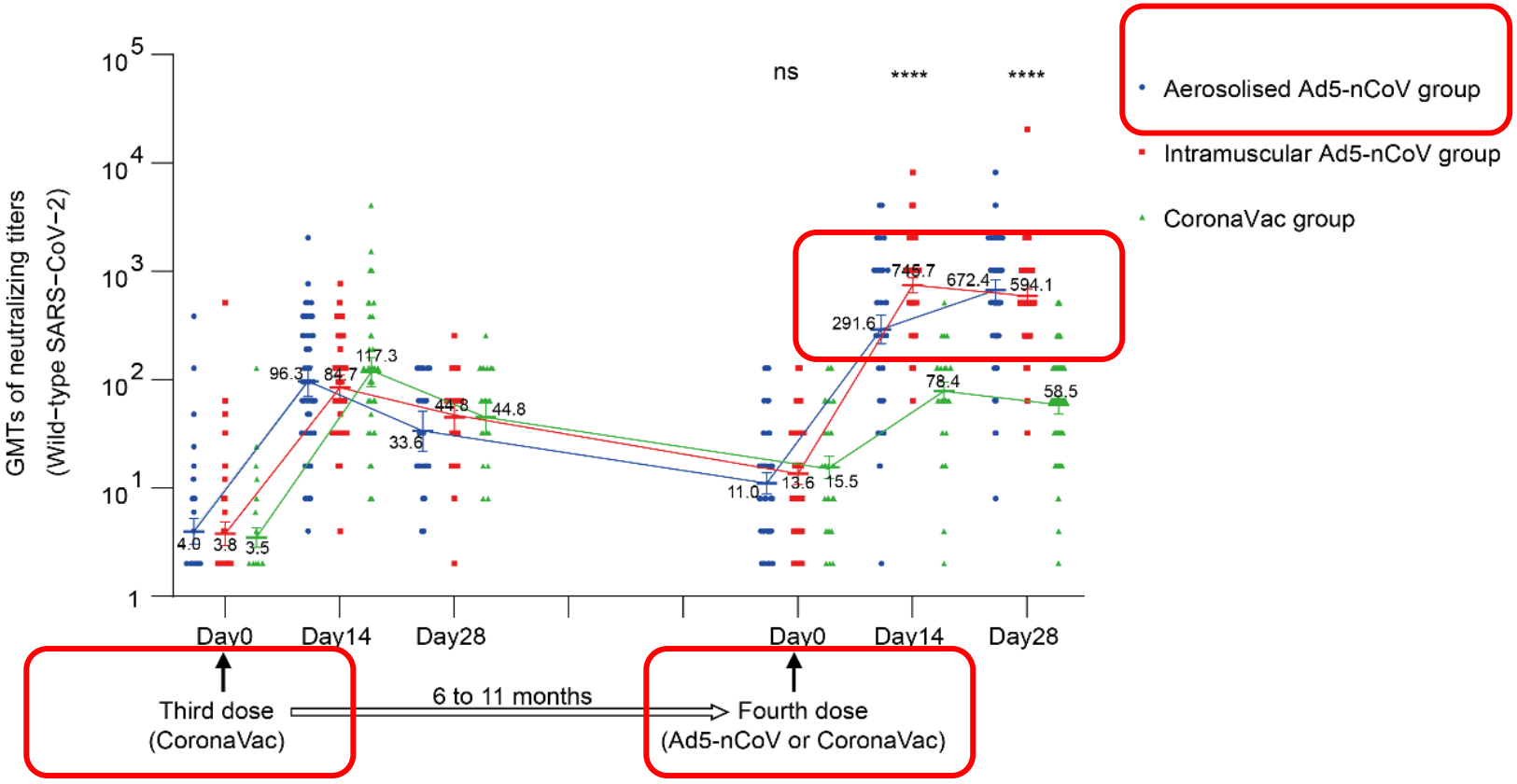


IL-2

Salivary sIgA positive ratio of in the aerosolized Ad5-nCoV group was significantly higher than that in the intramuscular injection of Ad5-nCoV group and CoronaVac group



Humoral immune responses were further enhanced using aerosolized Ad5-nCoV and intramuscular Ad5-nCoV heterologous boost

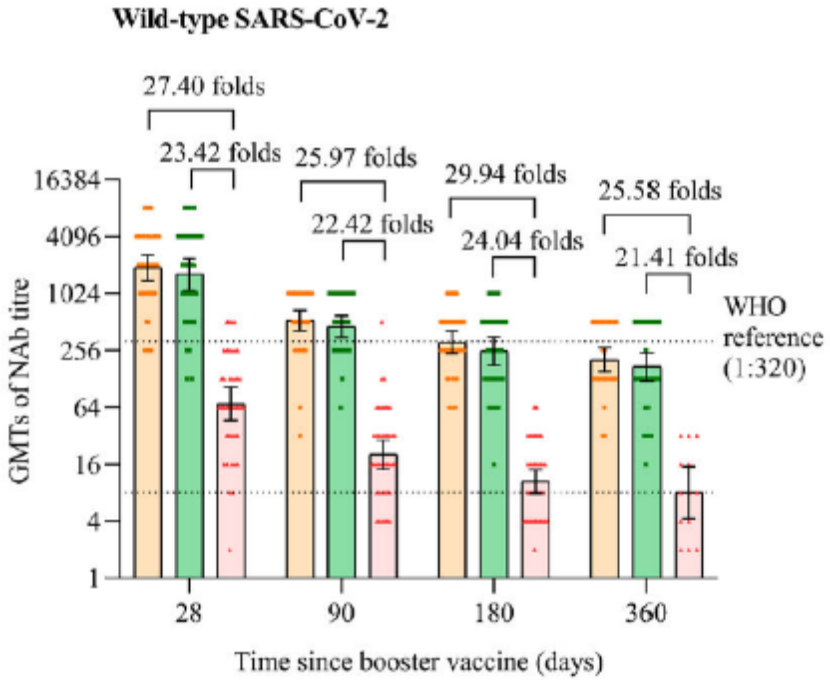


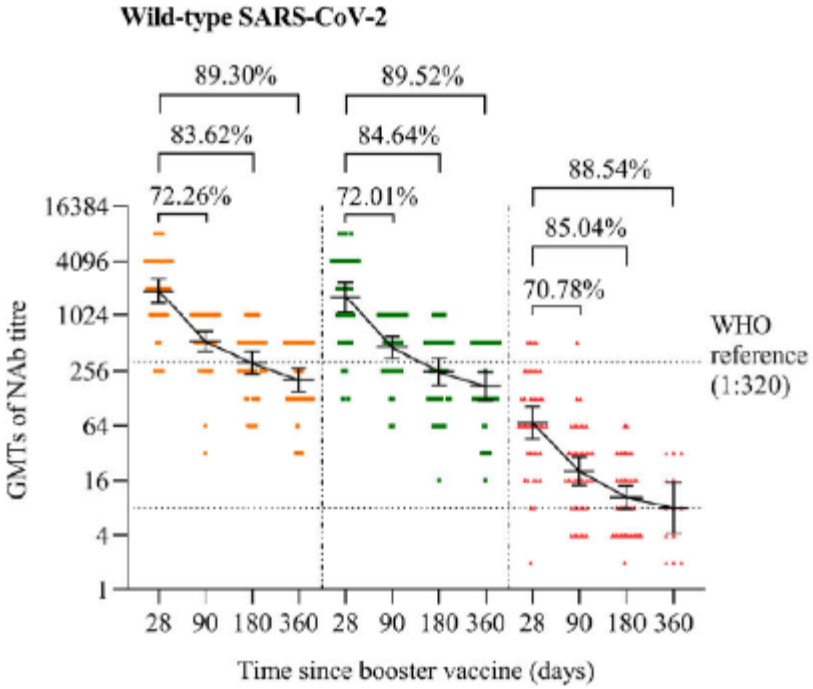
Real World Follow up Analysis of vaccine efficacy after One year

	Ad5-nCoV		CoronaVac		Hazard ratio (%)	Efficacy (95% CI)	p value
	N	No. of cases	N	No. of cases			
Total	8790	4766	197	136	64.9	35.1(23.0, 45.2)	<0.0001
Case type							
Antigen or PCR	8790	1618	197	58	56.4	43.6(26.7, 56.6)	<0.0001
Clinical cases*	7172	3148	139	78	69.6	30.4 (12.8, 44.4)	0.0016
Age group, years							
18-59	5767	3298	136	97	64.1	35.9 (21.5, 47.6)	<0.0001
≥60	3023	1468	61	39	67.3	32.8 (7.6, 51.1)	0.0145

Notes: N is the number of participants whose time and outcome are not missing in each group. * Presents participants whose time and outcome are not missing and without positive antigen rapid test or nucleic acid test results. Efficacy=1-HR. Cox regression analysis was used.

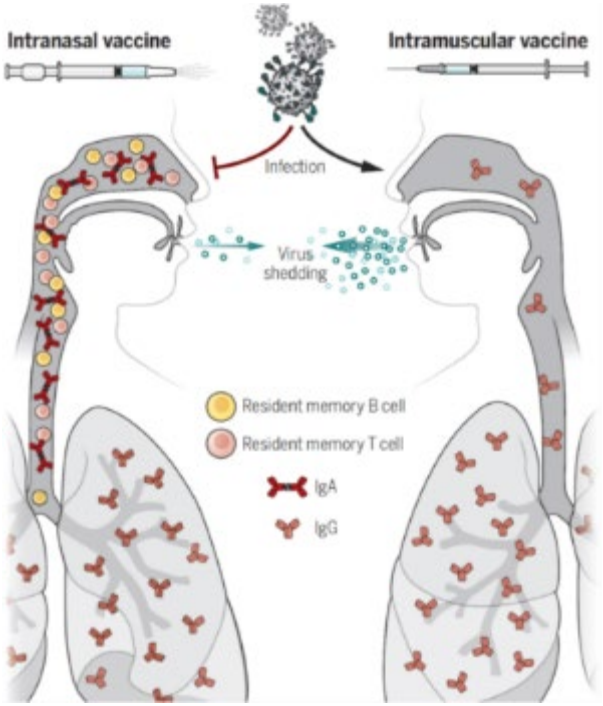
Nab after One year

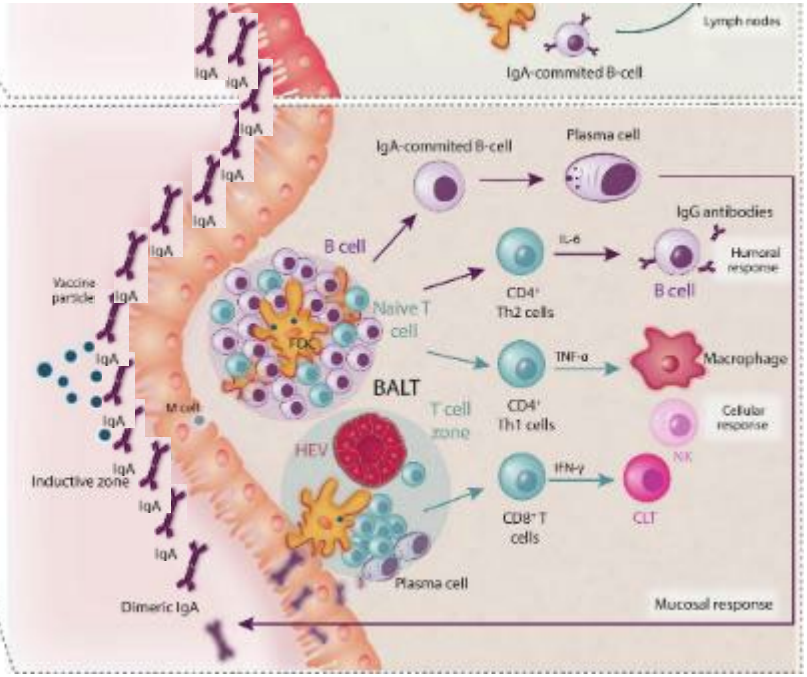




More Questions need to be addressed

How be fair to compare Nasal vs Inhale
Functional sIgA assay
Other biomarkers related mucosal response
How to design CHIM trials in current situation
…….





Adenovirus Vector Based Covid-19 Inhalation Vaccine

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