



Moving away from the
parenteral route:

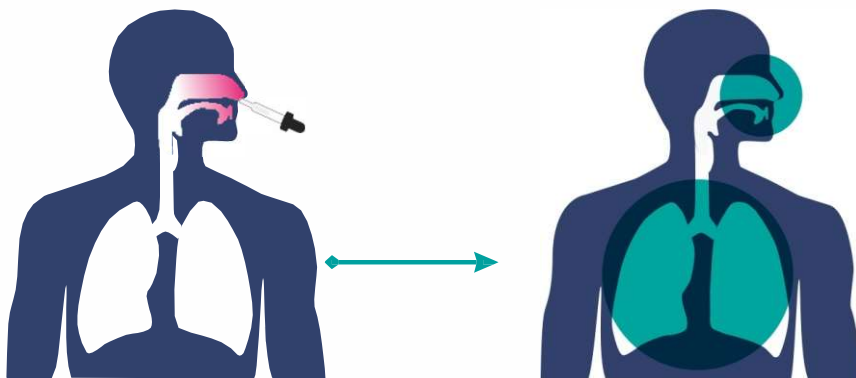
DEVELOPMENT OF BBV154: An intranasal SARS-CoV-2 vaccine

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Chief Development Officer

BBV154: AN INTRANASAL COVID-19 VACCINE

Nasal route has excellent potential for vaccination due to the organized immune systems of the nasal mucosa.

Intranasal SARS-CoV-2 Vaccines



Likely to
prevent
infection and
transmission

Likely to
prevent
disease

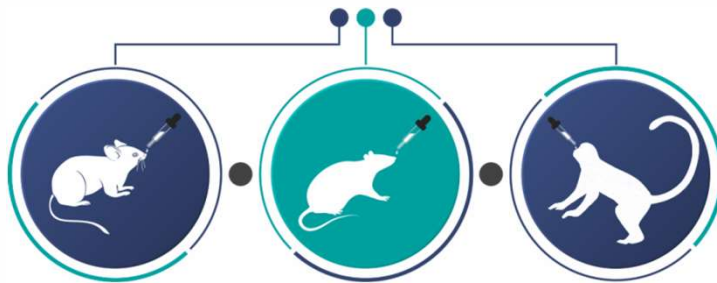
TARGET PRODUCT PROFILE

Product Attribute	Target
Indication	SARS-CoV-2 and emerging variants of concern
Active Ingredient	Replication Deficient ChAd vector expressing the stabilized Spike SARS-CoV-2 (Wuhan variant)
Dosage administration	Intranasal (Drops)
Dosage Form	Liquid Suspension with 0.5mL per dose
Dosage Regimen	Day 0 and Day 28
Target Population	Adults
Safety Profile	Tolerable safety profile in preclinical and clinical studies
Presentation	Multidose/ Single Dose
Storage	2-8 C
Shelf Life	2 Years



PRECLINICAL STUDIES

ANIMAL PROTECTIVE STUDIES



Mice

Hamsters

Rhesus Macaques



Vaccine induced antibodies
decreased viral clearance
in the upper & lower airway
(post viral challenge)

<https://doi.org/10.1016/j.cell.2020.08.026>

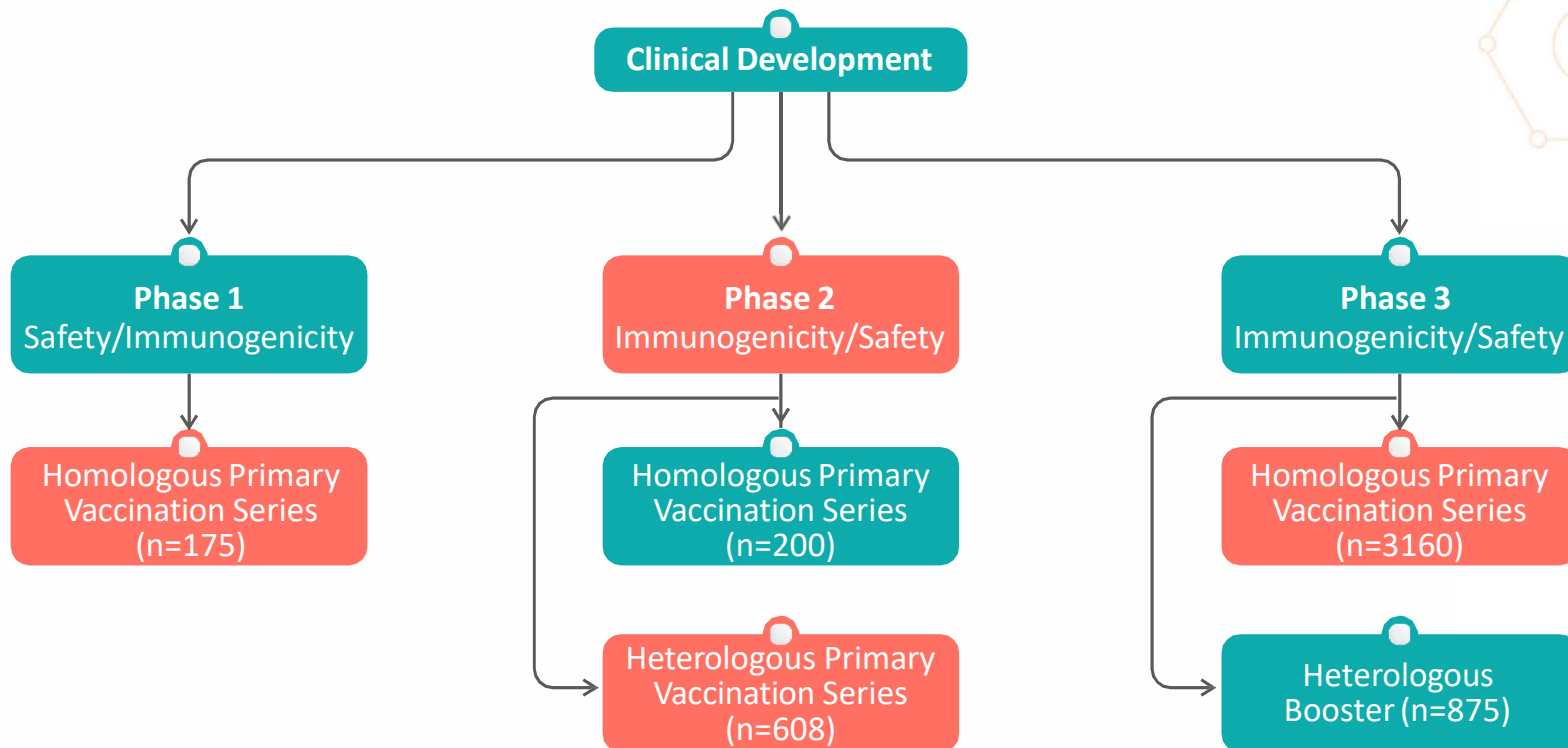
[https://www.cell.com/cell-reports/fulltext/S2211-1247\(21\)00798-1?returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2211124721007981%3Fshowall%3Dtrue](https://www.cell.com/cell-reports/fulltext/S2211-1247(21)00798-1?returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS2211124721007981%3Fshowall%3Dtrue)

<https://www.sciencedirect.com/science/article/pii/S266637912100046X>

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CLINICAL DEVELOPMENT PLAN



MANUSCRIPT AVAILABLE (OPEN ACCESS)

npj | vaccines



ARTICLE OPEN

Phase III Pivotal comparative clinical trial of intranasal (iNCOVACC) and intramuscular COVID 19 vaccine (Covaxin[®])

Chandramani Singh¹, Savita Verma², Prabhakar Reddy³, Michael S. Diamond⁴, David T. Curiel⁵, Chintan Patel⁶, Manish Kumar Jain⁷, Sagar Vivek Redkar⁸, Amit Suresh Bhate⁹, Vivek Gundappa¹⁰, Rambabu Konatham¹¹, Leelabati Toppo¹², Aniket Chandrakant Joshi¹³, Jitendra Singh Kushwaha¹⁴, Ajit Pratap Singh¹⁵, Shilpa Bawankule¹⁶, Raches Ella¹⁷, Sai Prasad¹⁷, Brunda Ganneru¹⁷, Siddharth Reddy Chiteti¹⁷, Sreenivas Kataram¹⁷ and Krishna Mohan Vadrevu¹⁷✉

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<https://www.nature.com/articles/s41541-023-00717-8>

STUDY HOMOLOGOUS PRIMARY VACCINATION SERIES (2-DOSES)

Phase 3 trial overview (CTRI/2022/02/040065)

Protocol Title	A Phase III randomized open label multi-center study to compare immunogenicity and safety of BBV154 with COVAXIN®, and to assess Lot to Lot Consistency of BBV154 in Healthy Volunteers.			
Study Groups	Cohorts/ Vaccine Candidates	Age groups	Dosage (D0, D28)	Sample Size (n)
Arm-I	BBV154	≥18 to ≤65 years	0.5 ml (intranasal)	3,000
Arm-II	COVAXIN		0.5 ml (injectable)	160
Endpoints	Reactogenicity, Unsolicited AEs, SAEs Immunogenicity (neutralizing antibody titers, CMI responses)– at one month intervals			
Primary Endpoint	Primary analysis for licensure is designed to demonstrate superiority of BBV154, based on GMTs of Neutralizing antibody titre on day 42 (2 weeks after the second dose).			
Study Duration	6-month study after the last vaccine administration.			

PRIMARY ENDPOINT

Neutralization Antibody Titers (PRNT₅₀)


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Day	Vaccine	n	GMT	(95% CI)	GMFR*	GMT ratio (BBV154:Covaxin)	
						Ratio	(95% CI)
Ancestral (Wuhan) virus – whole population							
Day 0	BBV154	481	26.1	(18.7-36.6)	-	0.7	(0.04-1.37)
	Covaxin®	159	37.0	(20.9-65.4)	-		p=0.30
Day 42	BBV154	481	768.5	(665.1-888.0)	29.4	1.5	(1.11-1.88)
	Covaxin®	159	531.0	(425.9-662.1)	14.4		p=0.006
Day 90	BBV154	481	843.2	(746.3-952.7)		1.2	(0.94-1.49)
	Covaxin®	159	712.7	(587.7-864.5)			p=0.15

BBV154 > COVAXIN

- Superior Serum Nabs
- Durable responses till month 3 & 6

PRIMARY ENDPOINT

BA.5 Neutralization Antibody Titers (PRNT₅₀)

Day	Vaccine	n	GMT	(95% CI)	GMFR*	GMT ratio (BBV154:Covaxin®)	
						Ratio	(95% CI) p value
Omicron BA.5							
Day 0	BBV154	159	10.2	(6.1-17.1)		2.4	(0.72-8.06)
	Covaxin®	50	4.2	(1.4-12.6)			
Day 42	BBV154	161	170.8	(137-213)	16.7	2.1	(1.18-3.64)
	Covaxin®	50	82.4	(48.9-139)	19.6		p=0.02

Superior Serum
Nabs to Omicron
BA.5

SPIKE SPECIFIC BINDING ANTIBODY TITERS ELISA

		n	GMT	(95% CI)	GMT ratio (BBV154:Covaxin)	
					Ratio	(95%CI)
Anti-S1 IgG (serum)						
Day 0	BBV154	481	3675	(3191- 4232)	1.2	(0.9- 1.6)
	Covaxin®	159	3090	(2435- 3922)		
Day 42	BBV154	481	7175	(6490- 7932)	1.3	(1.0- 1.5)
	Covaxin®	159	5689	(4952- 6537)		
Day 90	BBV154	481	8851	(8100- 9672)	1.1	(0.95- 1.33)
	Covaxin®	158	7866	(6824 9066)		
Anti-S1 IgA (serum)						
Day 0	BBV154	481	1978	(1754- 2230)	1.2	(0.9- 1.5)
	Covaxin®	159	1701	(1382- 2093)		
Day 42	BBV154	481	3069	(2794- 3371)	0.9	(0.74- 1.01)
	Covaxin®	159	3537	(3102- 40356)		
Day 90	BBV154	479	3670	(3400-3962)	1.3	(1.1-1.6)
	Covaxin®	158	2843	(2409-3354)		
Anti S1 secretory IgA (saliva)						
Day 0	BBV154	58	10.7	(8.4- 13.5)	1.3	(0.9- 2.1)
	Covaxin®	22	8.0	(5.4- 11.8)		
Day 42	BBV154	58	12.3	(8.7- 17.4)	1.9	(1.1- 3.0)
	Covaxin®	22	6.6	(4.6- 9.5)		
Day 90	BBV154	58	9.9	(7.5- 13.2)	0.8	(0.4, 1.4)
	Covaxin®	22	13.2	(7.6- 23.3)		

BBV154 Generated:

↑ Serum IgA

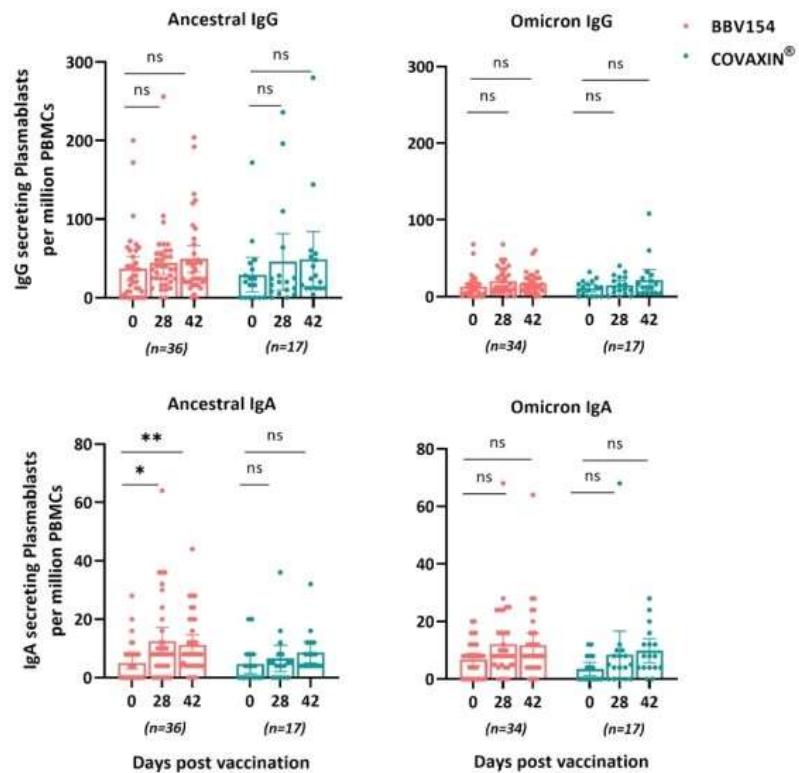
↑ Saliva IgA


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CELL MEDIATED RESPONSES

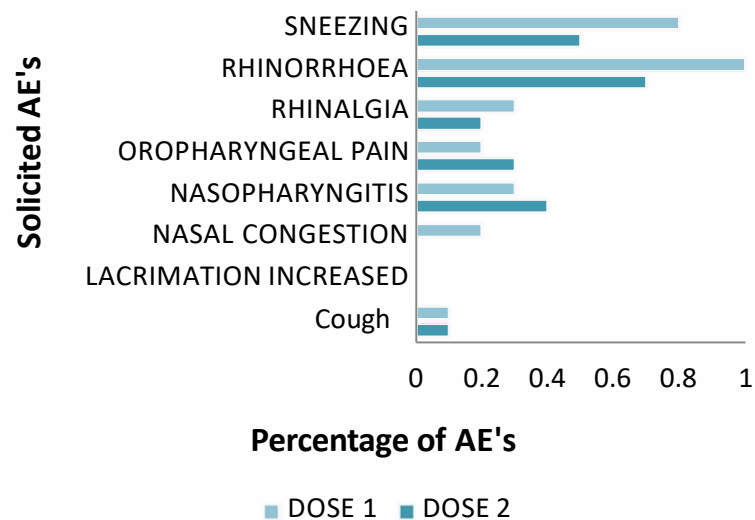
14 days after the last dose



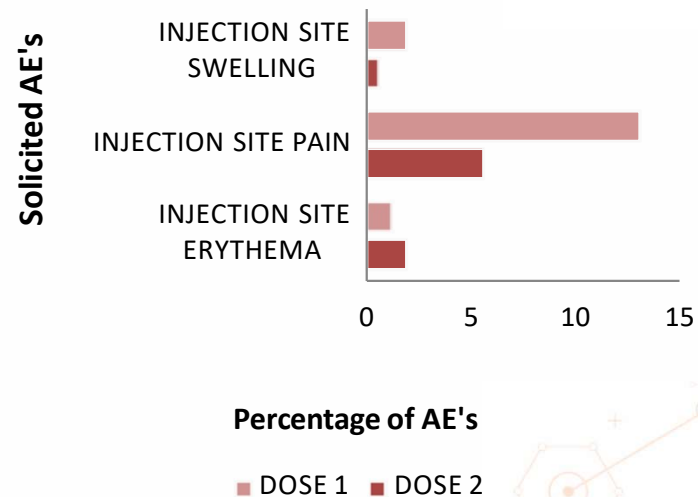
BBV154:
 ↑ IgA secreting
 Plasmablasts

SOLICITED ADVERSE EVENTS (LOCAL) 7 days after each dose

BBV154

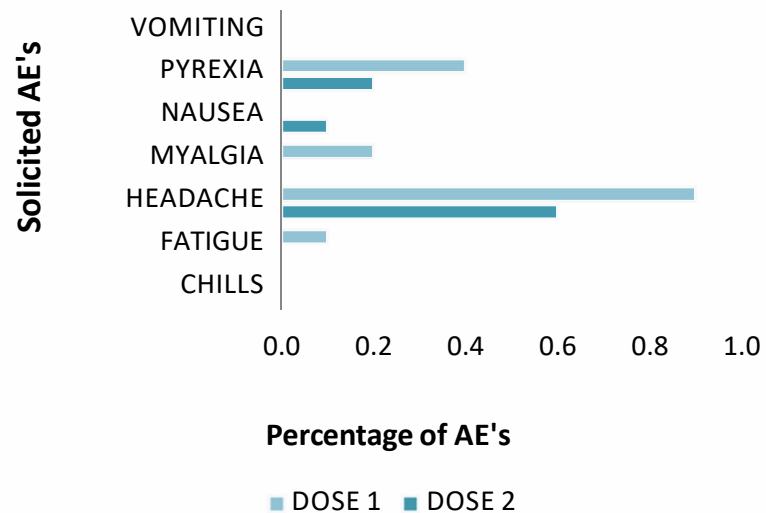


COVAXIN

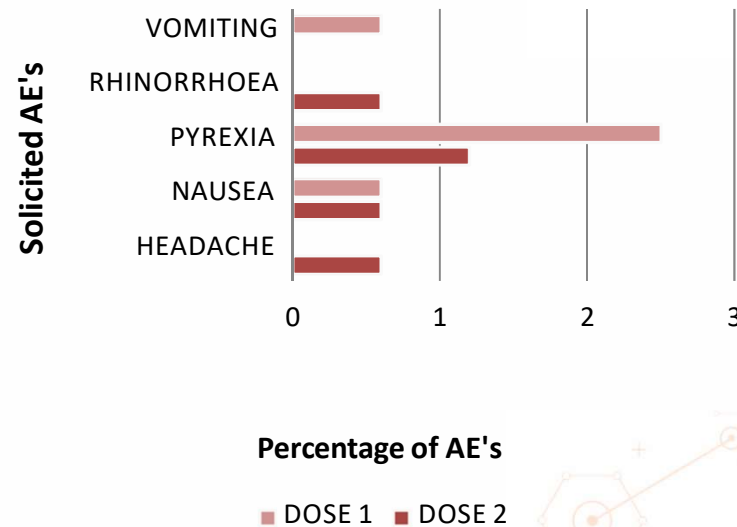


SOLICITED ADVERSE EVENTS (SYSTEMIC) 7 days after each dose

BBV154



COVAXIN



CONCLUSIONS



Preclinical data supports **vaccine effectiveness** and safety



Phase 1 and 2 data support safety and **durable immunogenic responses**



Meets all **reactogenicity and safety expectations** (6-12 months after second dose for 4,000 participants)



Immunological Superiority in Serum Nabs and Salivary IgA



Durable T and B Cell Responses



No cases of **VITT** till date



Consistent Manufacturing (lot to lot consistency)



Robust **AEFI** system in-place



Post Marketing safety underway



Trials for **Bivalent** boosters and effectiveness are being planned

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THANK YOU

