

Long Live
Immunity

SpikoGen[®]
COVID-19 Vaccine

SpikoGen[®]
COVID-19 Vaccine

Dr Saghar Barati
Clinical Pharmacist

Overview

Vaxine Pty
Ltd

SpikoGen[®]
COVID-19 Vaccine
formulation
and Advax[™]



Preclinical &
phase I clinical
studies

Phase II & III
clinical trials

Booster shot
trial

Vaxine Pty Ltd

- A rapidly growing Australian biotechnology company based in Adelaide.
- Much of its vaccine development is conducted in collaboration with global collaborators including:
 - The National Institutes of Health (NIH)
 - The United States Agency for International Development (USAID)



Vaxine Pty Ltd

Vaxine's human candidates:

- COVID-19
- Seasonal and pandemic influenza
- Hepatitis B
- Japanese encephalitis
- West Nile Virus
- Malaria
- Rabies
- Allergy



SpikoGen[®] Formulation

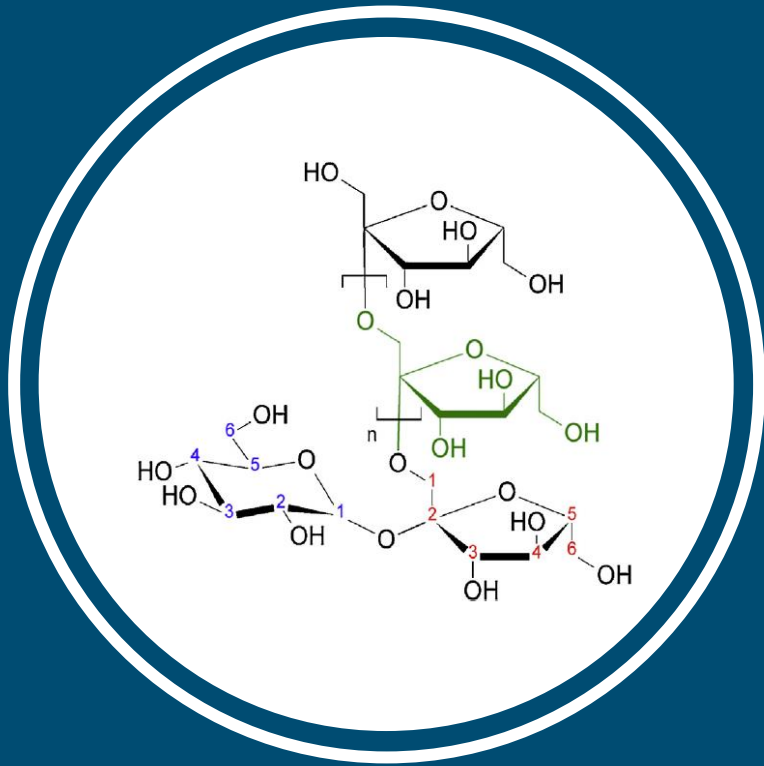
COVID-19 Vaccine



SARS-CoV-2-Spike
protein



Advax-SM
(Advax + CPG 55.2)



Advax™ adjuvants

Vaxine's lead product:

Advax™ range of adjuvants

Patent number: WO2012175518A1



Advax

Upregulates surface molecules involved in antigen presentation, T- and B-cell co-stimulation and chemotaxis including MHC class I and II, CD11c, CD80, and CD86

Attract additional monocytes to the site of antigen administration

Enhanced ability to present antigen to and activate B cell and CD4 and CD8 T-cells in the draining lymph node, with resultant memory T cell and plasma cell generation

Because
All Lives Matter


www.spkogen.com



Promotes the survival and proliferation of Th1 cells

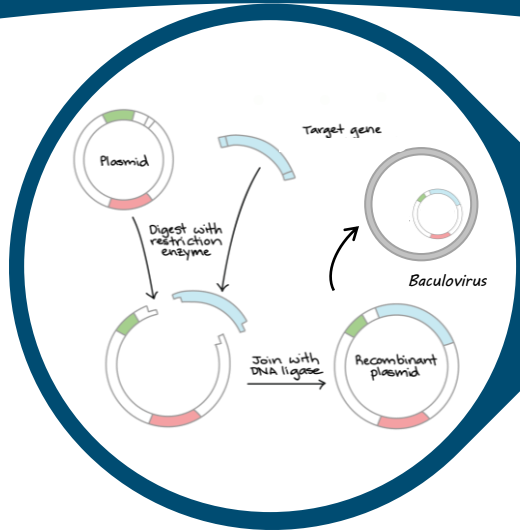
Enhances T follicular helper (Tfh) production of IL-21

Enhancing B-cell immunoglobulin production

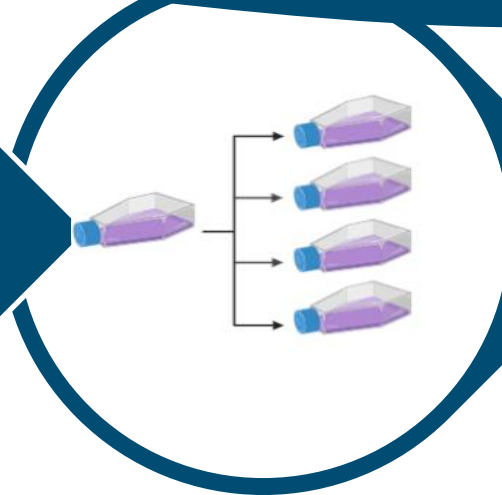
Enhance of humoral immunity as well as cellular immunity



SpikoGen[®], a protein subunit vaccine against COVID-19 produced in insect cells



Spike Protein gene cloned into baculovirus



Optimization of Insect Cell Expression System



Large scale bioreactor cell culture and protein purification

- Robust protein expression platform (also used for Cervarix, Flublok)

Immunisation of ferrets and mice with recombinant SARS-CoV-2 spike protein formulated with Advax-SM adjuvant protects against COVID-19 infection



Lei Li^{a,b,1}, Yoshikazu Honda-Okubo^{a,b,1}, Ying Huang^c, Hyesun Jang^c, Michael A. Carlock^c, Jeremy Baldwin^a, Sakshi Piplani^{a,b}, Anne G. Bebin-Blackwell^c, David Forgacs^c, Kaori Sakamoto^e, Alberto Stella^f, Stuart Turville^f, Tim Chataway^b, Alex Colella^b, Jamie Triccas^g, Ted M. Ross^{c,d,2}, Nikolai Petrovsky^{a,b,h,*,2}

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^e Department of Pathology, University of Georgia, Athens, GA, USA

^f Centre for Virus Research, Westmead Millennium Institute, Westmead Hospital and University of Sydney, Sydney 2145, NSW, Australia

^g School of Medical Sciences and Marie Bashir Institute, University of Sydney, Sydney, NSW 2006, Australia



Preclinical studies

Murine Study

- Key outcomes:

- C57BL/6 and BALB/C mice
- Vaccine is well tolerated
- Induction of neutralizing antibodies against wild type and alpha variant (cVNT and pVNT)
- Strong Th1 T-Cell Immunity



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^gSchool of Medical Sciences and Marie Bashir Institute, University of Sydney, Sydney, NSW 2006, Australia



Covax-19/Spikogen[®] vaccine based on recombinant spike protein extracellular domain with Advax-CpG55.2 adjuvant provides single dose protection against SARS-CoV-2 infection in hamsters

Lei Li ^{a,b}, Yoshikazu Honda-Okubo ^{a,b}, Jeremy Baldwin ^a, Richard Bowen ^c, Helle Bielefeldt-Ohmann ^d, Nikolai Petrovsky ^{a,b,*,*}

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^bCollege of Medicine and Public Health, Flinders University, Adelaide 5042, Australia

^cDepartment of Biomedical Sciences, Colorado State University, Fort Collins, CO 80523, USA

^dSchool of Chemistry & Molecular Biosciences, The University of Queensland, St. Lucia, Qld 4072, Australia

Preclinical studies

Ferret Challenge Study

- Key outcomes:

- Anti-RBD antibody response
- Protection against nasal virus shedding (sterilizing immunity)



Phase I Clinical Trial



Phase I Human Clinical Trial

(NCT04453852) commenced July 2, 2020



Healthy participants 18-65 years.

Forty subjects (30 Covax-19, 10 saline)



Evaluating **Safety** and **Tolerability**

Conclusion



Healing Hands,
Saving Lives

- ✓ Covax-19 was **safe** and **tolerable**
- ✓ Covax-19 was **immunogenic**
- ✓ There were not any abnormalities in lab data in the Covax-19 group
- ✓ Based on pre-clinical and phase 1 studies, Covax-19 could be a potential COVID-19 vaccine after evaluating its safety, immunogenicity and efficacy in phase 2 and 3 clinical trials

A brief report of Phase 2

A phase II, Randomized, Two-armed, Double-blind, Placebo controlled trial to evaluate safety and immunogenicity of an adjuvanted recombinant SARS-CoV-2 spike (S) protein subunit vaccine (SpikoGen[®]) produced by CinnaGen Co. (Two doses of 25µg with dosing interval of 21 days)

Target Sample Size: 400

Principal investigators:

Dr. Payam Tabarsi

Dr. Masoud Mardani Dashti

Keypoints of SpikoGen® Phase II study

- The study was performed on both seronegative and seropositive patients
- Definition of **seronegative** vs. **seropositive** patients
- Definition of **seroconversion** in both populations
- **ITT** VS. **PP** analysis



Save Life
Live Better



Seroconversion Results

on day 35 in pooled analysis

Immunogenicity Factor	SpikoGen [®]	Placebo	P-value
Seroconversion of neutralizing antibody (ELISA-based)	233 (78%)	17 (20%)	<0.001
Seroconversion of IgG against S protein	190 (64%)	6 (7%)	<0.001

GMFR Results

Fold rise in neutralizing antibody levels based on ELISA

2.90
in
Placebo

VS

20.01
in
SpikoGen[®]

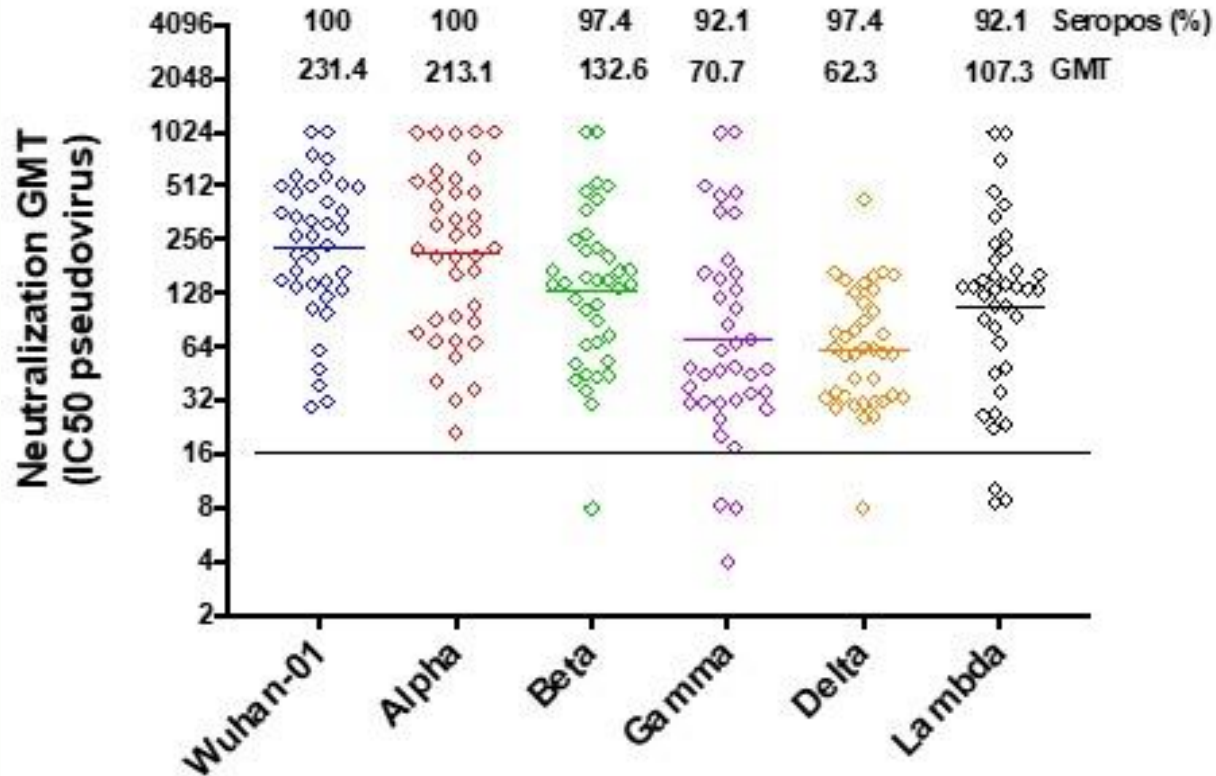
P-value <0.001

Conventional Virus Neutralizing Test (cVNT) Results

Immunogenicity Factor	Placebo	SpikoGen [®]	P Value
Conventional Virus Neutralizing Test (titer > 1:16)	25/83 (30%)	256/295 (87%)	<0.001

Absolute Effect in SpikoGen[®]: (82%)

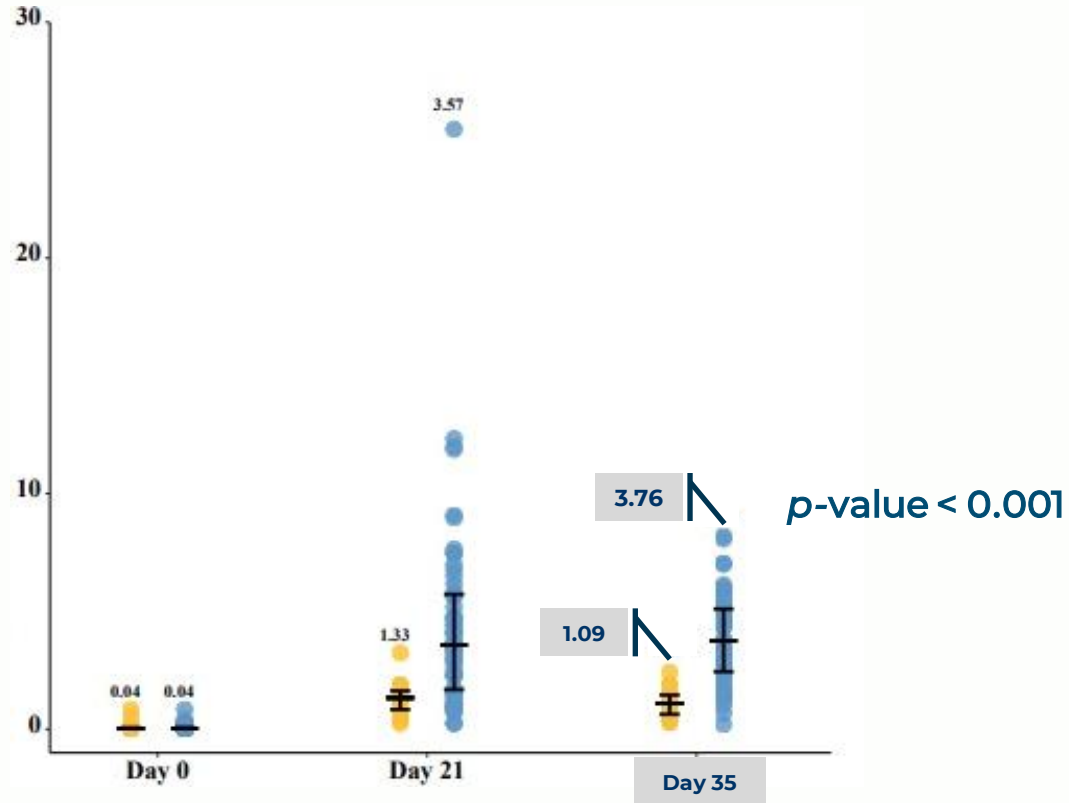
Cross-neutralization ability of samples from vaccinated subjects on day 35



Cellular immunity;

Fold rise in IFN- γ after stimulation with SARS-CoV-2-S CD4 epitope

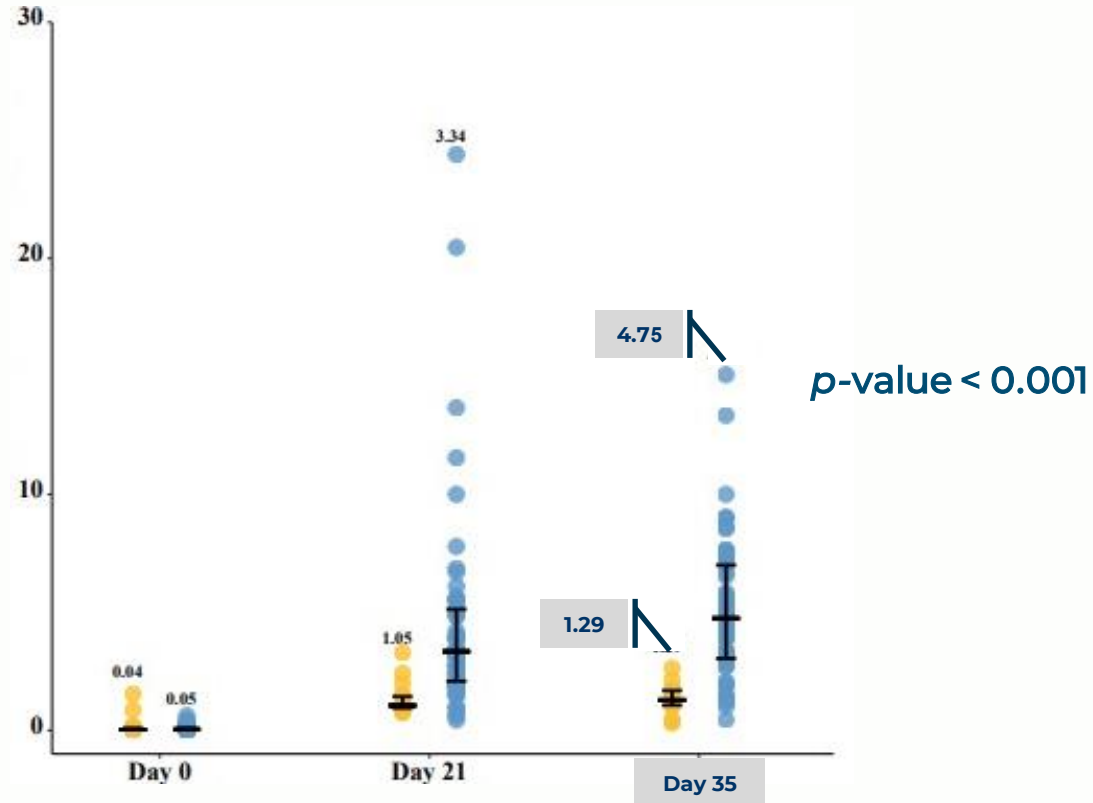
- SpikoGen[®]
- Placebo



Cellular immunity;

Fold rise in IFN- γ after stimulation with SARS-CoV-2-S CD4 & CD8 epitopes

- SpikoGen[®]
- Placebo



Safety Results

- **The most local solicited adverse event was injection site pain.**
- **The most systemic solicited adverse event was fatigue.**
- **There were no serious unsolicited adverse events and no abnormalities in blood and urine analysis.**

Phase 2 paper

The image shows a screenshot of a journal article page. At the top left, the journal logo 'CMI CLINICAL MICROBIOLOGY AND INFECTION' and 'ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES' are displayed. The top right navigation bar includes 'Log in', 'Register', 'Subscribe', 'Claim', a search icon, and a menu icon. Below the journal information, the article type 'ORIGINAL ARTICLE | ARTICLES IN PRESS' is shown. A row of icons for 'PDF [825 KB]', 'Figures', 'Save', 'Share', 'Reprints', and 'Request' is present. The main title of the article is 'Safety and immunogenicity of SpikoGen®, an advax-cpg55.2-adjuvanted sars-cov-2 spike protein vaccine: a phase 2 randomized placebo-controlled trial in both seropositive and seronegative populations'. Below the title, the authors are listed: 'Payam Tabarsi • Nassim Anjidani • Ramin Shahpari • ... Nikolai Petrovsky • Lei Li • Saghar Barati'. A 'Show all authors' link is provided. The publication date is 'Published: April 15, 2022' and the DOI is 'https://doi.org/10.1016/j.cmi.2022.04.004'. A 'PlumX Metrics' logo is visible in the bottom right corner. The background of the article content area features a faint, semi-transparent flowchart or diagram.

CMI CLINICAL MICROBIOLOGY AND INFECTION ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

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ORIGINAL ARTICLE | ARTICLES IN PRESS

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Safety and immunogenicity of SpikoGen®, an advax-cpg55.2-adjuvanted sars-cov-2 spike protein vaccine: a phase 2 randomized placebo-controlled trial in both seropositive and seronegative populations

Payam Tabarsi • Nassim Anjidani • Ramin Shahpari • ... Nikolai Petrovsky • Lei Li • Saghar Barati ✉

Show all authors

Published: April 15, 2022 • DOI: <https://doi.org/10.1016/j.cmi.2022.04.004>

PlumX Metrics

A brief report of Phase 3

A phase III, Randomized, Two-armed, Double-blind, Placebo controlled trial to evaluate efficacy and safety of an adjuvanted recombinant SARS-CoV-2 spike (S) protein subunit vaccine (SpikoGen®) produced by CinnaGen Co. (Two doses of 25µg with dosing interval of 21 days)

Target Sample Size: 16876

Principal investigators:

Dr. Payam Tabarsi

Dr. Masoud Mardani Dashti

Efficacy results

SpikoGen[®] Placebo		Parameter
0.2249		RR
77.51 (26.32-93.14)	PP population	Efficacy % (CI)



Safety Results

- The most local solicited adverse event was injection site pain.
- The most systemic solicited adverse event was fatigue.
- Safety follow up is still ongoing...

Medical history of the enrolled participants in phase 3 by SOC



At least one comorbidity at baseline

Placebo n (%)	SpikoGen® n (%)	System Organ Class
382 (9.05)	1147 (9.06)	Gastrointestinal disorders
312 (7.4)	1057 (8.35)	Psychiatric disorders
323 (7.66)	1028 (8.12)	Endocrine disorders
307 (7.28)	918 (7.25)	Respiratory, thoracic and mediastinal disorders
240 (5.69)	732 (5.78)	Hepatobiliary disorders
170 (4.03)	523 (4.13)	Skin and subcutaneous tissue disorders
149 (3.53)	462 (3.65)	Eye disorders
151 (3.58)	451 (3.56)	Blood and lymphatic system disorders
132 (3.13)	406 (3.21)	Cardiac disorders
128 (3.03)	378 (2.99)	Renal and urinary disorders
127 (3.01)	321 (2.54)	Reproductive system and breast disorders
0 (0)	3 (0.02)	Pregnancy, puerperium and perinatal conditions

At least one comorbidity at baseline

Placebo n (%)	SpikoGen® n (%)	System Organ Class
92 (2.18)	307 (2.43)	Immune system disorders
108 (2.56)	297 (2.35)	Vascular disorders
117 (2.77)	295 (2.33)	Nervous system disorders
102 (2.42)	291 (2.3)	Surgical and medical procedures
98 (2.32)	291 (2.3)	Musculoskeletal and connective tissue disorders
62 (1.47)	184 (1.45)	Neoplasms benign, malignant and unspecified (incl cysts and polyps)
48 (1.14)	153 (1.21)	Metabolism and nutrition disorders
33 (0.78)	103 (0.81)	Investigations
27 (0.64)	73 (0.58)	Infections and infestations
18 (0.43)	61 (0.48)	Ear and labyrinth disorders
7 (0.17)	19 (0.15)	Injury, poisoning and procedural complications
5 (0.12)	7 (0.06)	General disorders and administration site conditions

Preliminary results of SpikoGen[®] Booster shot study

The logo for SpikoGen COVID-19 Vaccine features the brand name 'SpikoGen' in a bold, blue, sans-serif font. A small, stylized virus particle icon is positioned above the letter 'i'. Below the brand name, the words 'COVID-19 Vaccine' are written in a smaller, blue, sans-serif font. The entire logo is set against a white background.

A Randomized, Two-armed, Double-blind, Placebo controlled (5:1) trial to evaluate immunogenicity and safety of an adjuvanted recombinant SARS-CoV-2 spike (S) protein subunit vaccine (SpikoGen[®]) produced by CinnaGen Co. (one dose of 25µg as a booster shot, 4-9 months after primary series)

Target Sample Size: 300

Principal investigators:

Dr. Payam Tabarsi

Dr. Masoud Mardani Dashti

A decorative geometric pattern in the bottom-left corner of the slide, consisting of several overlapping triangles in shades of blue and orange.

The study was performed on 3 different subgroups:



Save Life
Live Better

Participants whose primary vaccination were based on



Inactivated viruses



Viral vectors



Recombinant proteins



SpikoGen
COVID-19 Vaccine

Immunogenicity Results on day 14

GMC results of Neutralizing antibody (ELISA)	Day 0		Day 14*	
	SpikoGen®	Placebo	SpikoGen®	Placebo
Pooled population	3.26	3.98	61.37	5.35
SpikoGen®	4.55	2.45	51.57	3.57
Viral vector	4.84	6.15	69.24	6.92
Inactivated virus	2.41	4.07	62.06	5.68

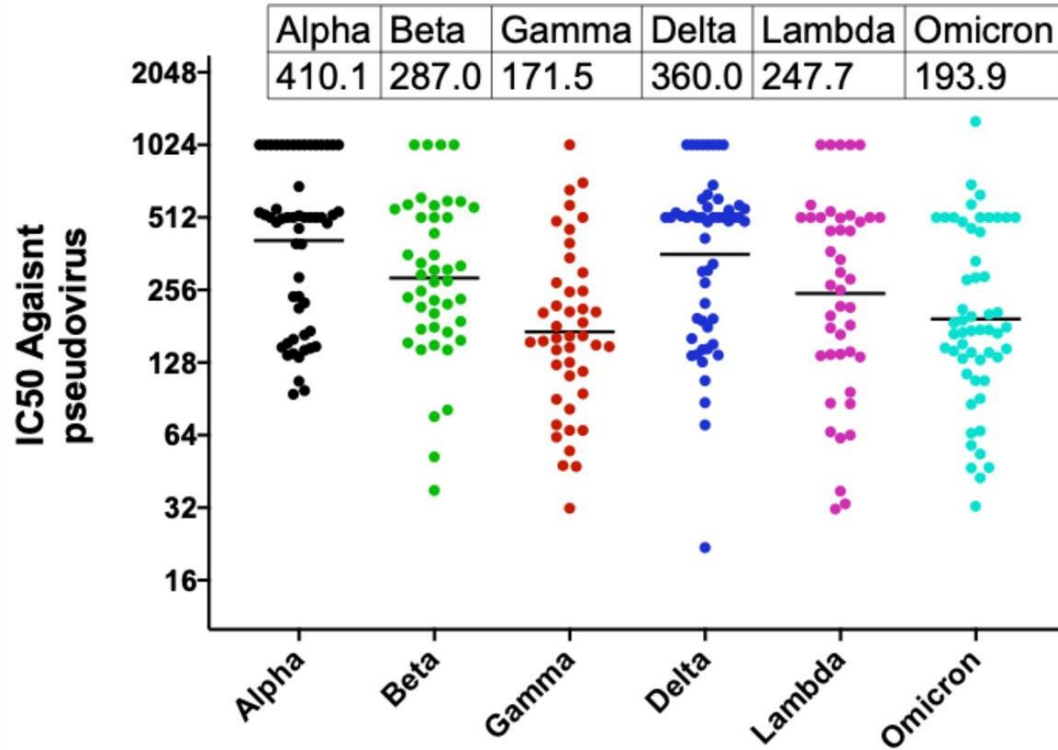
*all p -values < 0.05

Immunogenicity Results on day 14

GMFR results

SpikoGen®	Fold rise in neutralizing Ab (based on ELISA)	Placebo	P-value
Pooled population			
18.83	vs	1.34	<0.001
SpikoGen®			
11.33	vs	1.46	<0.001
Viral Vector			
14.32	vs	1.13	<0.001
Inactivated virus			
25.77	vs	1.4	<0.001

Cross-neutralization ability of samples from vaccinated subjects on day 14



Safety Results

- The most local solicited adverse event was injection site pain.
- The most systemic solicited adverse event was fatigue.
- Safety follow up is still ongoing...



Confirmatory results of SpikoGen[®] COVID-19 Vaccine booster shot in phase II

- Single dose of SpikoGen[®]
- Seropositive participants at baseline In phase II clinical trial of SpikoGen[®]
- Safe, with NO serious unsolicited adverse events

	SpikoGen [®]	Placebo	p-value
GMFR	12.11	1.93	<0.001
Confidence interval 95%	(8.86-16.56)	(1.49-2.5)	

Conclusion

- **Acceptable efficacy against Delta variant in preventing Severe forms (77.51%)**
- **Acceptable external validity**
- **Comparable safety profile to other COVID-19 vaccine trials**
- **a promising vaccine as a booster shot**
- **The trial is still ongoing...**

Other Ongoing trials

- **A non-inferiority clinical trial to compare the immunogenicity and safety of SpikoGen[®] in children aged 5-12, adolescents aged 12-18 and adults**
- **A clinical trial to evaluate the immunogenicity and safety of SpikoGen[®] in kidney transplant patients being fully vaccinated with Sinopharm vaccine**

Thanks for your Attention

SpikoGen[®]