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Journey of Whole Virion Inactivated SARS-CoV-2 Vaccine-Covaxin (BBV152) an Indigenous Vaccine of India

*Sutharson Lingadurai**

Department of Pharmacology, Nirmala College of Health Sciences, India

Abstract

Coronavirus Disease - COVID-19 was declared by WHO a pandemic due to wide spread contagious throughout the world and there was no treatment option in early 2020. Development of vaccine was the best preventive measure in any viral disease, in the line Covaxin (BBV152) an Indigenous vaccine of India was developed by Bharat Biotech International Ltd in association with Indian Council of Medical Research (ICMR). The development of Covaxin (Whole-Virion Inactivated Vero Cell derived) and screened successfully in preclinical and clinical studies. In this short communication, the author has put forwarded the complete journey of Covaxin (BBV152) and how successfully it come across. Recently it was found to be neutralizing the different variants too. DCGI has given nod for conduct of Phase II/III trial for the age group of 2 to 18 years category in May 2021.

COVID-19

Coronavirus Disease 2019 (COVID-19) outbreak happened in December 2019 and World Health Organization (WHO) has declared pandemic [1]. Corona virus or SARS-CoV-2 is a single-stranded RNA virus that belongs to the family *Coronaviridae*. Due to COVID-19 as on today 07th June 2021 about 174,038,004 are infected worldwide. In India 28,909,604 are infected and caused death of 349,229 and those who recovered are 27,150,727.

Covaxin (BBV152)

Vaccination is the best preventive tool for acting against any infectious disease. As per WHO as on today 102 COVID vaccine candidates are in clinical trial and 185 are in preclinical trial [2].

Covaxin (BBV152), an Indigenous product of India developed by Bharat Biotech in association with Indian Council of Medical Research (ICMR). It contain dead virus, to activate the immune system of our body for defensive role against specific antigen. Covaxin has to be stored at 2 to 8°C.

Components of Covaxin (BBV152)

1. Whole-virion inactivated SARS-CoV-2 antigen 6 µg of
2. Imidazoquinolinone15 µg,
3. 2-phenoxyethanol 2.5 mg,
4. 2 aluminum hydroxide gel (250 µg),
5. Phosphate buffer saline up to 0.5 ml [3].

Preclinical Studies

Immunogenicity and protective efficacy of BBV152 in Syrian hamster model

Syrian hamster was used as animal model, three whole virion inactivated vaccine candidates used [4].

Vaccine candidates have induced Coronavirus specific IgG after three dose vaccination regimes. IgG2 response was predominant in hamsters for all three candidates. The prognostic effect was observed in respiratory pathological conditions and improvement seen in short period of time. It confirms the immunogenic potential of vaccine candidates against SARS-CoV-2.

Immunogenicity and protective efficacy of inactivated BBV152 in rhesus macaques

In this study four groups of five macaques were used. Three vaccine candidates BBV152 A,B,C were treated 0 day and 14th day for three groups and fourth group received placebo to avoid bias related with solvents/adjuvants and SSARS- CoV-2 was challenged on 14th day after administration

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Correspondence:
Sutharson Lingadurai, Department of Pharmacology, Nirmala College of Health Sciences, Chalakudy, Thrissur, Kerala, 680311, India, Tel: +91 9746012400;
E-mail: sutharson709@gmail.com

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of vaccine candidates. It was observed that IgG2 mediated neutralizing antibodies from 3rd week of treatment. Broncho alveolar lavage fluid, nasal swab, throat swab and lung tissues shown significant improvement from viral load after 3rd week in the vaccinated macaques. There was no evidence of Pneumonia related impacts in interstitial fluid of Lungs and histological and immunochemistry studies for the BBV152 A, B and C treated groups whereas it was clearly shown the phenomenon of pneumonia for placebo group in all parameters. The study results provided a benchmark impact for BBV152 for fighting against Coronavirus [5].

Th1 skewed immune response of BBV152 and its safety evaluation

BBV152 was studied for safety and Immunogenicity in rodents (mice, rats and rabbits) in dose ranges (3 μg and 6 μg) with two different adjuvants. The study results depicted vaccine candidates generated significant level of Neutralizing Antibody titers (NAb), at both concentrations, in all three rodents with highest safety parameters. BBV152 administered rodents produced elevated level of IgG2 and produced more production of coronavirus-specific IFN-γ+CD4+ T lymphocyte response [6].

Clinical Studies

BBV152 (Covaxin) received Drug Controller General of India (DCGI) nod for Phase I & II Clinical studies in July, 2020.

Phase I

Method adopted:

Study design: The trial was designed to avoid bias from the concern by adopting Randomized, Double blind, Multi centric method to ascertain the safety and immunogenicity of Covaxin in eleven hospitals across India. Healthy adults of age varying from 18 to 55 years are chosen by investigator. Individuals with positive COVID-19 tests were excluded. The trial was registered with clinical trial NCT04471519. The participants of the trial were given Informed consent and all procedures have been duly approved by Institutional Human Ethics Committee, they were administered randomly either one of the three vaccines by intramuscular route on 0 day and 14th day. The outcomes of vaccine treated patients were noted time to time till the end of study [7].

Outcome: After analyzing the Phase I result it was found that Covaxin has better safety and produced enhanced immune responses.

Phase II

Method Adopted:

Study Design: Same as like Phase I trial was designed for phase 2 clinical trial to evaluate the immune inducing ability and safety of Covaxin in healthy adults of age group 12 to 65 years and trial executed at 9 hospitals across India [3].

Outcome: The results from the phase 2 study revealed that Covaxin induces both cell-and humoral mediated immunity. There were no differences in neutralizing antibodies in genders and different age groups found. It was observed that no serious adverse effects of Covaxin reported during this study.

Phase III

Method Adopted:

Study design: Double blind, Randomized, Multicentric and placebo-controlled study was performed. The study was performed to evaluate the safety and efficacy of Covaxin about 25,800 participants [8].

Outcome: The result of Phase III Study demonstrated 81% interim efficacy of Covaxin in preventing COVID-19.

Neutralization of UK-variant VUI-202012/01 with COVAXIN vaccinated human serum

Plaque reduction neutralization test was conducted from the recipients of Covaxin against hCoV-19/India/20203522 (UK-variant) and hCoV27 19/India/2020Q111 (heterologous strain). A Covaxin neutralized significantly UK-variant and the heterologous strain [9].

Neutralization of variant under investigation B.1.617 with sera of BBV152 vaccines

Covaxin neutralized VUI B.1.617 from 12 isolates in VeroCCL81 cells [10]. As the studies are in progress further detailed studies to confirm the clinical efficacy against B.1.617 variant.

Neutralization of B.1.1.28 P2 variant with sera of natural SARS-CoV-2 infection and recipients of BBV152 vaccine

Two-doses of Covaxin enhanced the IgG titer and neutralized both B.1.1.28.2 and D614G variants [11].

DCGI approves Phase II/III clinical trial of Covaxin in the age group of 2 to 18 Years

As per recommendation of subject expert committee, DCGI gave nod for conduct of Phase II/III trial for Covaxin in the age group of 2 to18 years in India [12].

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