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COVAXIN -BHARAT BIOTECH: MINI REVIEW

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ABSTRACT

Bharat Biotech is a pioneering biotechnology company known for its world -class Research & Development and manufacturing capabilities in medical field. The company's mission is to deliver affordable, safe and high quality vaccines and bio-therapeutics that help people prevail over diseases. Bharat Biotech creates innovative vaccines and bio-therapeutics trusted by physicians around the world. Bharat biotech International limited(BBIL) has developed vaccines for influenza HINI , Rota virus , Japanese Encepalitis(JENVAC®), Rabies , Chikungunya ,Zika ,Cholera , and the world 's first tetanus toxoid conjugated vaccine for typhoid . The current article focuses on India's first indigenous vaccine Bharat Biotech COVAXIN® against COVID-19, its development and product efficiency. Bharat Biotech COVAXIN® vaccine was developed in collaboration with the Indian Council of Medical Research (ICMR) - National institute of Virology (NIV). Covaxin is a two -dose vaccine, with the second dose required to be given 28 days after the first dose of the vaccine. The vaccine has shown 81% efficacy in preventing Covid -19 during the phase 3 trial. So India is now self-sufficient in vaccine development and has developed vaccine Covaxin and is effectively working to fight against Corona virus. Covaxin was considered safe and generated immune response without any serious side effects, according to the interim results.

KEYWORDS: Covaxin, COVID-19, Bharath Biotech, Clinical Trials.

1. INTRODUCTION

Bharat Biotech International limited (BBIL) is located in Genome valley, Hyderabad, India, a hub for the global biotech industry. BBIL has built a world class vaccine and bio therapeutics, research and product development, Bio safety Level 3 manufacturing, and vaccine supply and distribution. The company owns 145 patents and their products help people in over 123 countries. The company living to its fullest potential has delivered more than 5 billion doses of vaccines worldwide.

BBIL 's commitment to the global social innovation programs and the public - private partnership resulted in introducing path breaking World Health Organisation (WHO) pre-qualified vaccines such as BIOPOLIO ® , ROTAVAC®, ROTAVAC® 5D , AND Typbar TCV® combating polio , rota virus , typhoid infections , respectively . Novel vaccines against malaria and tuberculosis are under development through global partnerships. The acquisition of chiron Behring Vaccines has positioned BBIL as the world's largest rabies vaccine manufacturer with Chirorab® and Indirab®.

There was a new public health crises threatening the world with the emergence and spread of 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus originated in bats and was transmitted to humans through yet unknown intermediary animals in Wuhan, Hubei province, China in December 2019. There have been around 96,000 reported cases of

coronavirus disease 2019 (COVID-2019) and 3300 reported deaths to date (05/03/2020). The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 d. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, malaise among others. The disease is mild in most people; in some (usually the elderly and those with comorbidities), it may progress to pneumonia, acute respiratory distress syndrome (ARDS) and multi organ dysfunction. The current study aims at developments and features of Covaxin against COVID -19 introduced by Bharat biotech.

2. COVAXIN

COVAXIN®, India's indigenous COVID-19 vaccine by Bharat Biotech is developed in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV)The indigenous, inactivated vaccine is developed and manufactured in Bharat Biotech's BSL-3 (Bio-Safety Level 3) high containment facility.
The vaccine is developed using Whole-Virion Inactivated Vero Cell derived platform technology. Inactivated vaccines do not replicate and are therefore unlikely to revert and cause pathological effects. They contain dead virus, incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection.

COVAXIN® is included along with immune-potentiators, also known as vaccine adjutants, which are added to the vaccine to increase and boost its immunogenicity. It is a 2-dose vaccination regimen given 28 days apart. It is a vaccine with no sub-zero storage, no reconstitution requirement, and ready to use liquid presentation in multi-dose vials, stable at 2-8^{o}c.

C0VAXIN® − India's 1st Indigenous COVID-19 vaccine, demonstrated 77.8% vaccine efficacy against symptomatic COVID-19 disease. COVAXIN® has proven to neutralize the variants - B.1.1.7 (Alpha), P.1- B.1.1.28 (Gamma) & P.2 - B.1.1.28 (Zeta), B.1.617 (Kappa), B.1.351 & B.1.617.2 (Beta & Delta).

COVAXIN® demonstrated **77.8%** vaccine efficacy against symptomatic COVID-19 disease, through evaluation of 130 confirmed cases, with 24 observed in the vaccine group versus 106 in the placebo group. The efficacy against severe symptomatic COVID-19 disease is shown to be **93.4%**. The efficacy data demonstrates **63.6%** protection against asymptomatic COVID-19.

Safety analysis demonstrates adverse events reported were similar to placebo, with 12% of subjects experiencing commonly known side effects and less than 0.5% of subjects feeling serious adverse events.

Table 1 - Covaxin publications list

Sl. No	Published	Title	Journal
1	Phase 1 Human Clinical Trial	Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomized, phase 1 tr	THE LANCENT infectious Diseases
2	Hamster Efficacy Study	Immunogenicity and protective efficacy of BBV152, whole virion inactivated SARS CoV-2 vaccine candidates in the Syrian hamster model	Cell Press
3	Non-Human Primate Efficacy Study	Immunogenicity and protective efficacy of inactivated SARS-CoV-2 vaccine candidate, BBV152 in rhesus macaques	Nature communications
4	Phase 2 Human Clinical Trial	Safety and immunogenicity clinical trial of an inactivated SARS-CoV-2 vaccine, BBV152 (a phase 2, double-blind, randomized controlled trial) and the persistence of immune responses from a phase 1 follow-up report	THE LANCENT infectious Diseases
5	Pre clinical Safety and Immunogenicity	Th1 Skewed immune response of Whole Virion Inactivated SARS-CoV-2 Vaccine and its safety evaluation	Cell Press
6	Neutralization of UK Variant (B.1.1.	Inactivated COVID-19 vaccine BBV152/COVAXIN effectively neutralizes recently emerged B.1.1.7 variant of SARS-CoV-2	Journal of Travel Medicine
7	Neutralization of Brazil variant of concern P2 (B.1.1.28)	Neutralization of B.1.1.28 P2 variant with sera of natural SARS-CoV-2 infection and recipients of BBV152vaccine	Journal of Travel Medicine
8	Neutralization of South Africa Variant (B.1.351) and Delta Variant (B.1.617.2	Neutralization against B.1.351 and B.1.617.2with sera of COVID-19 recovered cases and vaccines of	Journal of Travel Medicine

		BBV152	
9	Neutralization of Double mutant (B.1.617)	Neutralization of variant under investigation B.1.617with sera of BBV152 vaccines	Clinical Infectious Diseases
10	Phase 3 Human Clinical Trial	Efficacy, safety, and lot to lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): interim results of a randomized, double-blind, controlled, phase 3 trial	THE LANCENT infectious Diseases
11	COVAXIN® against Delta & Omicron variants	Covaxin's (BBV152) Vaccine Neutralizes SARS-CoV-2 Delta and Omicron variants	medRxiv
12	COVAXIN® Clinical Trial in Pediatric cohort 2 to 18 years	Immunogenicity and safety of an inactivated SARS-CoV-2 vaccine(BBV152) in children from 2 to 18 years of age: an open-label, age-de-escalation phase 2/3 study	THE LANCENT infectious Diseases
13	COVAXIN® Vaccine Effectiveness Study	SARS-CoV-2 Reinfection Rate and Estimated Effectiveness of the Inactivated Whole Virion Vaccine BBV152 Against Reinfection Among Health Care Workers in New Delhi, India	JAMA OEN NETWORK
14	COVAXIN® efficacy in Hamsters against Delta and Omicron variants	Protective efficacy of COVAXIN® against Delta and Omicron variants in hamster model	BIORXIC
15	Cell mediated immune responses of COVAXIN®	Inactivated whole-virion vaccine BBV152/Covaxin's elicits robust cellular immune memory to SARS-CoV-2 and variants of concern	NATURE MICROBIOLOGY
16	COVAXIN® Booster Study	Persistence of immunity and impact of third dose of inactivated COVID-19 vaccine against emerging variants	NATURE SCIENTIFIC REPORTS

3. COVAXIN – CLINICAL TRIALS

The Pre-clinical studies demonstrated strong immunogenicity and protective efficacy in animal challenge studies conducted in hamsters & non-human primates. The vaccine received Drug Controller General of India (DCGI) approval for Phase I & II Human Clinical Trials in July, 2020.

In Phase 2 study, 380 participants of 12-65 years were enrolled. COVAXIN® led to tolerable safety outcomes and enhanced humoral and cell-mediated immune responses. A total of 25,800 subjects have been enrolled and randomized in a 1:1 ratio to receive the vaccine and control in a Event-Driven, randomized, double-blind, placebo-controlled, multi centre phase 3 study. The purpose of this study is to evaluate the efficacy, safety, and immunogenicity of COVAXIN® in volunteers aged ≥18 years. Of the 25,800 participants, >2400 volunteers were above 60 years of age and >4500 with co morbid conditions.

A total of 375 subjects have been enrolled in the Phase 1 study and generated excellent safety data without any reactogenicity. Vaccine-induced neutralizing antibody titers were observed with two divergent Severe Acute Respiratory Syndrome CoronavirusSARS-CoV-2 strains. Percentage of all the side-effects combined was only 15% in vaccine recipients.

Covaxin's Phase I, II and III trails involved 25,800 participants aged between 18 and 98 across 25 sites.To ensure generalisation of the results, this study included participants from diverse geographic locations, enrolling 380 participants across nine hospitals across nine states in India. The trial is being called the largest clinical trial ever conducted in India.

The vaccines that were given to the people did not show any serious side effects. The participants of phase 1 trial after long term also did not show any side effects and they were tolerated. The common side effect of phase 2 trial done on people was pain in the infection site, headache, fatigue, and fever. There were no serious illness occurred that was not reported. The gap were given between the phase 1 trial and phase2 trail that is about 3 months and when cell mediated response observed it showed neutralizing antibodies in phase 1 participants at 104 day and the level of the panel of convalescent serum were similar.

CONCLUSION

India's first indigenous vaccine against COVID-19, Covaxin, is safe and generates immune response without any serious side effects, according to the interim results. The vaccine has shown 81% efficacy in preventing Covid -19 during the phase 3 trial, which was conducted on 25,800 participants between 18-98 years of age, 2,433 over the age of 60 and 4,500 with co-morbidities. Research stated that vaccine induced binding and neutralizing antibody responses. The vaccine was given to lakhs of people, and there were hardly any side effects shown. No deaths has been caused by Covaxin so far.

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