COVID-19 Vaccine: Clinical Trials and Tribulations

Dr. Raches Ella
Project Lead  SARS-CoV-2 Vaccines
Types of Vaccines

Whole Inactivated

- Conventional and Safe Vaccine
- Used in Pregnancy
- In use for Decades

Vaccines
- Polio
- Pertussis
- S. Flu
- Rabies
- Japanese Encephalitis

www.bharatbiotech.com
VERO CELL MANUFACTURING PLATFORM

Developed several inactivated Vero cell derived vaccines which are proven, time-tested and long-lasting. A few include:

- **ROTAVAC**<sup>®</sup> ORAL ROTAVIRUS VACCINE 116E, LIVE ATTENUATED
- **JENVAC**<sup>®</sup> PURIFIED, INACTIVATED JAPANESE ENCEPHALITIS VACCINE
- **INDIRAB**<sup>®</sup> PURIFIED, INACTIVATED RABIES VACCINE

**ONGOING VACCINE CANDIDATE USING VERO CELL PLATFORM**

- CHIKUNGUNYA
- ZIKA
- sIPV
- BBV152* (COVAXIN)

- ~25 CLINICAL STUDIES
- ~300,000 SUBJECTS
- 15 YEARS EXCELLENT CLINICAL TRIAL SAFETY
- ~300 MILLION DOSES SUPPLIED FROM VERO MANUFACTURING PLATFORM
- EXCELLENT POST MARKETING SAFETY RECORD

[www.bharatbiotech.com](http://www.bharatbiotech.com)
BBV 152 : BSL3 PRODUCTION FACILITY

- Designed and constructed during 2017 – 2019
- Facility audited by ICMR technical team 2019
- Designed for large scale manufacturing and testing
COVAXIN™ PROGRESS

DEVELOPMENT

ANIMAL STUDIES

MOUSE, RABBITS, RATS

MONKEYS/HAMSTERS

CLINICAL TRIALS

PHASE 1
375 subjects

PHASE 2
380 subjects

PHASE 3
25,800 subjects

Initiated
STUDY DESIGN

THREE MODELS

Rats

Mice

Rabbits

Neutralizing Antibody Titer [MNT_{3}] (Log_{10} Scale)

Day 0  Day 7  Day 14  Day 21

6μg Ag + Algel  3μg Ag + Algel-IMDG  6μg Ag + Algel-IMDG  HCS

%CD3^{+} IFN-γ, T lymphocytes

%CD4^{+} IFN-γ, T lymphocytes

%CD8^{+} IFN-γ, T lymphocytes
Preclinical Evaluation of Live Viral Challenge Studies

NON-HUMAN PRIMATES & HAMSTER STUDIES
TWO BBV152 PAPERS
(UNDERGOING PEER-REVIEW)

Remarkable immunogenicity and protective efficacy of BBV152, an inactivated SARS-CoV-2 vaccine in rhesus macaques


DOI: 10.21035/rs.3.rs-65715/v1  Download PDF

Immunogenicity and protective efficacy of BBV152: a whole virion inactivated SARS CoV-2 vaccine in the Syrian hamster model


DOI: 10.21035/rs.3.rs-76768/v1  Download PDF
1. NON-HUMAN PRIMATE – STUDY DESIGN

- A 2-dose vaccination regimen of inactivated SARS-CoV-2 vaccine candidates was administered in 20 rhesus macaques (divided into four groups equally).

- One group was administered with placebo while three groups were immunized with 3 different vaccine candidates at 0 and 14 days. All the macaques were exposed to viral challenge 14 days after the 2nd dose.
LOAD OF COVID-19 SUBGENOMIC VIRAL RNA DETECTION IN RESPIRATORY TRACT SPECIMENS

**Upper airway protection**

**Nasal Swab**

![Graph showing viral copies/mL over days post-challenge for Nasal Swab with different groups indicated by markers.]

**Throat Swab**

![Graph showing viral copies/mL over days post-challenge for Throat Swab with different groups indicated by markers.]

**Lower airway protection**

**Bronchoalveolar lavage (BAL) gRNA**

![Graph showing viral copies/mL over days post-challenge for BAL gRNA with different groups indicated by markers.]

**BAL gRNA Lung Lobes**

![Graph showing viral copies/mL for BAL gRNA Lung Lobes with different lung lobes indicated.]

*Markers and colors indicate different groups and conditions: Placebo 6µg, + Algel, 3µg Algel-IMDG, 6µg Algel-IMDG.*
2. HAMSTER CHALLENGE - STUDY DESIGN

- Thirty-six female Syrian hamsters were divided into four groups of 9 hamsters each. Each group were immunized with 0.1 ml of PBS/vaccine formulations intramuscularly on 0, 14, and 35 days.
- The immunized hamsters were challenged with 0.1 ml of 105.5 TCID50 SARS-CoV-2 virus intranasally on the 8th-week post-immunization (day 50).

Three Dose Regimen Hamsters n=9/group

1. Placebo-PBS
2. 6μg + Algel 1
3. 3μg + Algel 2
4. 6μg + Algel 2

PBS, Phosphate-buffered saline; TCID50, 10 fold serial dilutions of 10^{5.5} Median Tissue Culture Infectious Dose
LOAD OF COVID-19 SUBGENOMIC VIRAL RNA DETECTION IN RESPIRATORY TRACT SPECIMENS

Upper airway protection

Nasal Wash gRNA

Throat Swab gRNA

Lower airway protection

Lungs gRNA

Trachea gRNA

www.bharatbiotech.com
**STATUS UPDATE & MILESTONES**

**PHASE I**
- **IM study:**
  - Administered at 14 day interval
  - 375 subjects.
- **ID study:**
  - Administered in 24 subjects.
- **Status:** Completed

**PHASE II**
- **IM study:**
  - Administered at a 28-day interval.
  - Includes 380 subjects.
  - Dose-1 has been administered.
- **ID study:**
  - Administered in 100 subjects.
- **Status:** Initiated

**PHASE III**
- Scheduled to commence in October all over India around 25 centers
- Trial includes >25,000 subjects
- IM study with 2-dose vaccine regimen administered at a 28-day interval.
- **Status:** To initiate

www.bharatbiotech.com
# Phase 1 trial overview (NCT04471519)

<table>
<thead>
<tr>
<th>Protocol Title</th>
<th>Phase 1, double blind, multi-centre study of safety, reactogenicity, tolerability, and immunogenicity in 375 healthy volunteers.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study Groups</strong></td>
<td><strong>Cohorts/Vaccine Candidates</strong></td>
</tr>
<tr>
<td>BBV152A</td>
<td>≥18 to ≤55 years</td>
</tr>
<tr>
<td>BBV152B</td>
<td></td>
</tr>
<tr>
<td>BBV152C</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Participants of either gender of age between ≥18 to ≤55 years.</td>
</tr>
<tr>
<td><strong>Study Endpoints</strong></td>
<td>Safety (Mild AEs were noted within 2 hours after Dose 1. No immediate AEs were reported after Dose 2). Immunogenicity (e.g., neutralizing antibody titers are suggestive of protection)</td>
</tr>
<tr>
<td><strong>Study Duration</strong></td>
<td>12-month follow up study after the last vaccine administration.</td>
</tr>
</tbody>
</table>
PHASE 1 & 2: GEOGRAPHIC SPREAD

List of Hospitals Across India

- All India Institute of Medical Sciences, Delhi
- Rana Hospital and Trauma Center, Gorakhpur
- All India Institute of Medical Sciences, Patna
- Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak
- Prakhar Hospital, Kanpur
- Gillukar Multispeciality Hospital, Nagpur
- Redkhar Hospital, Dhargalim VP
- Jeevan Rekha Hospital, Belgaum
- Institute of Medical Sciences and SUM Hospital, Bhubaneshwar
- Nizam Institute of Medical Sciences Hospital, Hyderabad
- SRM Hospital & Research Center, Chennai
A PHASE 2 STUDY SHOWING WHOLE-VIRION INACTIVATED SARS-CoV-2 VACCINE (BBV152) IN HEALTHY VOLUNTEERS

<table>
<thead>
<tr>
<th>Phase 2 trial overview (NCT04471519)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protocol Title</strong></td>
</tr>
<tr>
<td><strong>Study Groups</strong></td>
</tr>
<tr>
<td>BBV152A</td>
</tr>
<tr>
<td>BBV152B</td>
</tr>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td><strong>Study Endpoints</strong></td>
</tr>
<tr>
<td><strong>Study Duration</strong></td>
</tr>
</tbody>
</table>
Covaxin update: Bharat Biotech gets nod from DCGI panel for Phase III trials

The human trials of Covaxin have begun at the All India Institute of Medical Sciences.
THANK YOU