Medicines Control Authority of Zimbabwe

Clinical Trials Registry

PUBLIC TITLE/ACRONYM	
Scientific Title	A Phase I/II Study to Evaluate the Safety, Reactogenicity and Immunogenicity of RBD SARS-CoV-2 HBsAg VLP Vaccine in Healthy Adults

Primary Sponsor Details

Sponsors *	Serum Institute of India

Secondary Sponsor Details

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Countries of Recruitment *

Zimbabwe

Source of Funds	
Health Condition(s) or Problem(s) Studied *	Severe acute respiratory syndrome coronavirus 2 - SARS-CoV-2 (Covid-19)
Medicine Name *	RBD SARS-CoV2 HBsAg VLP Vaccine (SA) and RBD SARS-CoV2 HBsAg VLP VaccineBivalent; WT + SA)
Quantity of medicine required *	5000

7.0 PRINCIPAL INCLUSION CRITERIA *

1. Male or Female aged 18+ years
    1. Phase I: Subjects aged 18 to 45 years (both inclusive)
    2. Phase II: Subjects aged 18 and older (Strata 1: 18 to 59 years, Strata 2: 60 years and older; with equal distribution among each stratum. If an exact equal distribution between the two age strata is not possible, then a nearly equal distribution will be acceptable after obtaining approval from SIIPL)
2. Healthy participants as determined by medical history, physical examination, vital signs and clinical laboratory examination with no clinically significant deviations as judged by the Investigator at screeningand randomization (Day 0)
3. Test negative for SARS-CoV-2 infection by RT-PCR test at screening
4. Test negative for SARS-CoV-2 IgG antibody by serology test at screening

Capable and willing to provide written informed consent prior to the performance of any study-specific procedures

7.1 PRINCIPAL EXCLUSION CRITERIA *

1. Receipt of medications or vaccines intended to prevent or treat COVID-19 infection in the past
2. Fever (non-axillary temperature > 37.5 ºC) or any other symptoms of infection that have not completely resolved including respiratory symptoms/illnesses within the past 3 days from randomization (Day 0)
3. Participants with a BMI > 35 kg/m2.

BMI is to be calculated by the following formula: subject weight at baseline divided by subject height in meters multiplied by the subject height in meters. The numerical result will be rounded to the nearest 0.1.

1. Presence of current active viral or bacterial infection, at screening and randomization (Day 0), which is determined by the Investigator to be of clinical significance
2. Phase I only: Individuals with history of any major pulmonary, cardiovascular, renal, neurological, metabolic, gastrointestinal, hepato-biliary, blood dyscrasia, uncontrolled hypertension and diabetes, clinically significant chronic pulmonary disease, asthma (with the exception of history of resolved childhood asthma), immunological and autoimmune diseases or any condition which in the opinion of the Investigator might interfere with the evaluation of the study objectives.

Phase II only: Participants with clinically significant chronic cardiovascular, endocrine, gastrointestinal/ hepatic, renal, neurological, respiratory, immunological and autoimmune diseases or any other condition that are assessed by the Investigator as being clinically unstable within the prior 4 weeks evidenced by: a) hospitalization for the condition, including day surgical interventions, b) new significant organ function deterioration, c) needing addition of new treatments or major dose adjustments of current treatments

1. Individuals currently working in occupations with high risk of exposure to SARS-CoV-2 (e.g., healthcare worker in direct care of COVID-19 patients, front line workers in COVID-19 hotspots/outbreak areas)
2. Pregnant or lactating women or willingness/intention to become pregnant during the study.
3. Men and Women (of childbearing* potential) not agreeing to use adequate contraception** during the study.
4. Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the Investigator, contraindicate intramuscular injection.
5. Severely immunocompromised subjects. This exclusion category comprises a) subjects with solid organ transplantation; b) subjects with bone marrow transplantation; c) subjects under chemotherapy/radiotherapy; d) subjects with primary immunodeficiency; e) treatment with any anticytokine therapies. f) treatment with oral or intravenous steroids defined as daily doses of 10mg prednisolone or equivalent for longer than 3 months from the time of screening, or probable use of oral or intravenous steroids in the following four weeks
6. History of solid or non-solid malignancy or lymphoma (except basal cell carcinoma of the skin and cervical carcinoma in situ)
7. Known allergy to any component of the RBD SARS-CoV-2 HBsAg VLP Vaccine, or serious adverse reactions to the vaccine, such as urticaria, dyspnea, and angioedema.
8. A history of anaphylaxis to a vaccine, food, drug, toxin or other exposure.
9. Known hypersensitivity reactions to yeast.
10. Positive test result at screening for hepatitis B surface antigen, or hepatitis C virus antibody.
11. Clinical laboratory tests of blood and urine not within the normal range and show clinically relevant deviations as judged by the Investigator.
12. History of demyelinating disease or Guillain Barre syndrome
13. Eczema or other significant skin lesion or infection at the site of vaccination
14. Planned or actual receipt of any vaccine other than the study intervention within 30 days before and after each study vaccination
15. Positive screen for drugs of abuse# or alcohol (breath test) at screening and randomization (Day 0).
16. Participants who currently smoke 10 cigarettes or equivalent per day
17. Subjects not willing to/unable to comply with study procedures.
18. Participating in any other study and have received any other investigational medication or device within 30 days prior to randomization or are taking part in a non-medication study which, in the opinion of the Investigator, would interfere with the interpretation of the assessments in this study.
19. Receipt of blood/blood products/immunoglobulins or donation of blood/ blood products 8 weeks prior to vaccination or planned receipt or donation during the study period
20. Any other medical condition which in the opinion of the Investigator may affect the subject's safety or study participation and conduct

7.2 PRIMARY END POINTS *

PHASE 1: **PRIMARY ENDPOINTS**

- Incidence, severity, and relationship of immediate adverse events (IAE) within 30 minutes following each vaccination.
- Incidence, severity, and relationship of local and systemic solicited reactions up to 7 days following each vaccination.
- Incidence, severity, and relationship of unsolicited AEs up to 28days following each vaccination.
- Incidence, severity, and relationship of serious adverse events (SAEs)up to 28days following each vaccination.
- Incidence, severity, and relationship of unsolicited AEs through out the duration of the study (i.e. tillDay180 for Schedule A and Day 270 for Schedule B).
- Incidence, severity, and relationship of serious adverse events (SAEs)through out the duration of the study (i.e. tillDay180 for Schedule A and Day 270 for Schedule B).

PHASE 2: PRIMARY IMMUNOGENICITY ENDPOINTS

- Geometric mean titers of SARS-CoV-2 specific neutralizing antibodies against SARS-CoV-2 virus through Day 56 following first vaccine administration,
- Geometric mean titers of anti-SARS-CoV-2 IgG antibodies through Day 56 following first vaccine administration,
- Geometric mean fold rise in SARS-CoV-2 specific neutralizing antibodies against SARS-CoV-2 virus from baseline through Day 56 following first vaccine administration,
- Number of participants who seroconverted through Day 56 following first vaccine administration,

Note: Seroconversion is defined as a ≥ 2-fold change in SARS-CoV-2 specific neutralizing antibody titer from baseline

- Geometric mean titers (GMT) of SARS-CoV-2 specific neutralizing antibodies against SARS-CoV-2 virus through 28 days following third dose of study vaccine.
- Geometric mean titers of anti-SARS-CoV-2 IgG antibodies through 28 days following third dose of study vaccine.
- Geometric mean fold rise (GMFR) in SARS-CoV-2 specific neutralizing antibodies against SARS-CoV-2 virus from baseline (Day 0) through 28 days following third dose of study vaccine.
- Number of participants who seroconverted through 28 days following third dose of study vaccine.

Note: Seroconversion is defined as a ≥2-fold change in SARS-CoV-2 specific neutralizing antibody titer from baseline (Day 0)

PHASE 2: PRIMARY SAFETY ENDPOINTS

- Incidence, severity, and relationship of immediate adverse events (IAE) within 30 minutes following each vaccination.
- Incidence, severity, and relationship of local and systemic solicited reactions up to 7 days following each vaccination.
- Incidence, severity, and relationship of unsolicited AEs up to 28days following each vaccination.
- Incidence, severity, and relationship of serious adverse events (SAEs)up to 28days following each vaccination.
- Incidence, severity, and relationship of unsolicited AEs through out the duration of the study (i.e. tillDay180 for Schedule A and Day 270 for Schedule B).

Incidence, severity, and relationship of serious adverse events (SAEs)through out the duration of the study (i.e.tillDay 180 for Schedule A and Day 270 for Schedule B).

EXPLORATORY ENDPOINTS

- Number of participants with laboratory confirmed SARS-CoV-2/COVID-19 infectiontillDay 180 after first vaccination for Schedule A and Day 270 after fist vaccination for Schedule B.
- Cytokines response to CD8+ and CD4+ including T-Cell activity [(Th2 responses (IL5, IL13, IL4) and Th1 (IFNg and TNFa)] against SARS-CoV-2 RBD, to be measured by ELISPOT or standard assay

Schedule A: Baseline, Days 28, Day 56 and Day 84

Schedule B: Baseline, Days 28, Day 56 and prior to the 3rd dose and 28 days following third dose of study vaccine.

Active Control: Baseline, Days 28, and Day 56.

9.0 DESIGN OF THE TRIAL

Type of trial *	Controlled

If controlled

Randomised	Yes

Single Blind	No
Double Blind	No
Parallel group	
Cross over	
Other	
If yes to other, specify	
If controlled, specify the comparator	Covishield Vaccine (Astrazenaca Vaccine) manufactured by SIIPL
Other medicinal product(s)	No
Placebo	No
Other	
If yes to other, specify	
Other	

Expected Number of participants in Zimbabwe *	654
Total enrolment in each site: (if competitive enrolment, state minimum and maximum number per site.) *	Cumulative enrollment across sites
Total participants worldwide *	654

Time period for the trial *	Two years