RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN REKOMBINAN PROTEIN FUSI SARS-COV-2 (V-01)
PRODUKSI LIVZON MABPHARM INC. CHINA
SEBAGAI VAKSIN BOOSTER PADA DEWASA

Informasi Umum

1. *Recombinant SARS-CoV-2 Fusion Protein Vaccine* (V-01) merupakan vaksin dengan platform protein subunit yang telah terdaftar pada WHO Landscape of Candidate Vaccine dengan pengembang *Guangdong Provincial Center for Disease Control and Prevention/Gaozhou Center for Disease Control and Prevention.*
2. Uji klinik fase I dan fase II telah dilaksanakan di Cina. Uji klinik fase III telah mendapatkan PPUK dari Badan POM tanggal 19 Oktober 2021, yang dilaksanakan multicenter dan multinasional di Indonesia, Filipina, Rusia, Rwanda, Uganda, Ghana dan Mesir dengan merekrut sekitar 22.500 subjek (2000 subjek untuk studi imunogenisitas), untuk Indonesia akan merekrut 5.000 subjek.
3. Saat ini sponsor mengajukan uji klinik booster *Recombinant SARS-CoV-2 Fusion Protein Vaccine (V-01)* untuk 10.722 subjek yang telah mendapatkan vaksin primer inactivated (BBIBP-CorV atau CoronaVac). Di Indonesia akan merekrut sekitar 3000 subjek.

Informasi Uji Klinik

1.	Judul Protokol	:	***A Global, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Phase III Clinical Study to Evaluate the Efficacy, Safety, and Immunogenicity of Sequential Immunization of Recombinant SARS-CoV-2 Fusion Protein Vaccine (V-01) Against COVID-19 in Healthy Adults Aged 18 Years and Older after the Vaccination of 2 Doses of Inactivated Vaccines*** Nomor protokol: TG2102V01 Version 2.0 tanggal 9 Oktober 2021
2.	Produk Uji	:	Vaksin Rekombinan Protein Fusi SARS-COV-2 (V-01) 10 mcg diberikan 1 kali secara intramuskular
3.	Produk Pembanding	:	Placebo diberikan 1 kali secara intramuskular
4.	Center / Peneliti	:	1. Fakultas Kedokteran Universitas Islam Negeri Syarif Hidayatullah / dr. Hari Hendarto, PhD, SpPD-KEMD, FINASIM 2. RSUP Sanglah / DR. Dr. I Made Susila Utama, SpPD-KPTI FINASIM
5.	Sponsor / ORK	:	Livzon Mabpharm Inc. China / PT. Equilab International
6.	Persetujuan Etik	:	Belum mendapat persetujuan etik
7.	Desain Uji Klinik	:	*Global, multicenter, randomized, double-blind, placebo-controlled, phase III clinical study.*
8.	Jumlah Subjek	:	*10,772 subjects*
9.	Tujuan Uji Klinik	:	*Primary Objective* *Efficacy: To evaluate the relative efficacy of recombinant severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) fusion protein vaccine (V-01) as a booster to prevent symptomatic and reverse transcription polymerase chain reaction (RT-PCR) positive coronavirus disease 2019*

(COVID-19) (mild or above severity) compared with the placebo control group.

Safety: To evaluate the incidence of adverse events (AEs) within 28 days after the booster vaccination.

Secondary Objectives:
Efficacy:

- *To evaluate the relative vaccine efficacy of V-01 as a booster to prevent severe or above COVID-19 compared with the placebo control group.*
- *To evaluate the relative vaccine efficacy of V-01 as a booster to prevent symptomatic and RT-PCR positive COVID-19 (mild or above severity) in different age subgroups compared with the placebo control group*
- *To evaluate the relative vaccine efficacy of V-01 as a booster to prevent suspected but not confirmed COVID-19 compared with the placebo control group.*
- *To evaluate the relative vaccine efficacy of V-01 as a booster to prevent death caused by COVID-19 compared with the placebo control group.*
- *To evaluate the relative vaccine efficacy of V-01 as a booster to prevent hospitalization caused by COVID-19 compared with the placebo control group.*

Safety: To evaluate the incidence of serious adverse events (SAEs) and adverse events of special interest (AESIs) within 12 months after the booster vaccination.

Immunogenicity (immunology subgroup only): To *evaluate* the immunogenicity of V-01.

Exploratory objectives:

- *To explore the genotype of SARS-CoV-2 in symptomatic and RT-PCR positive COVID-19 cases.*
- *To explore the immunogenicity of V-01 against new SARS-CoV-2 variants.*

10. Kriteria Eligibilitas : ***Inclusion criteria:***

1. *Voluntarily participate in the study and sign the informed consent form.*
2. *Adults aged 18 years and older at time of consent, male or female.*
3. *Able to and willing to comply with study procedure based on the assessment of the investigator.*
4. *Participants who have completed the second dose of 2-dose regimen of inactive vaccination (BBIBP-CorV or CoronaVac) against SARS-CoV-2 in the past 3-6 months (Note: Participants who received mixed vaccination of BBIBP-CorV and CoronaVac will not be enrolled).*
5. *Healthy participants or participants with pre-existing stable medical conditions (A stable medical condition is defined as a disease not requiring significant change in therapy or hospitalization for worsening disease within 3 months before enrollment).*
6. *Males of reproductive potential and females of childbearing potential voluntarily agree to take effective and acceptable contraceptive methods from the signing of informed consent form to 3 months after vaccination; and a female participant of childbearing potential should*

have a negative pregnancy test at screening and on the day of vaccination (day 0).

Female participants of non-childbearing potential may be enrolled in the study. Non-childbearing potential is defined as surgically sterile (history of bilateral tubal ligation, bilateral oophorectomy, hysterectomy) or postmenopausal (defined as amenorrhea for ≥ 12 consecutive months prior to screening without an alternative medical cause).

Exclusion criteria:

1. *History of previous COVID-19 infection.*
2. *Positive for SARS-CoV-2 test by RT-PCR during screening period (Note: Participants can be enrolled in the study and receive the investigational product without waiting for the report of the SARS-CoV-2 test by RT-PCR).*
3. *History of severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and other human coronavirus infections or diseases.*
4. *History of severe allergy to any vaccine, e.g., acute allergic reactions, urticaria, skin eczema, dyspnea, angioneurotic edema or abdominal pain etc., or be allergic to any components of V-01.*
5. *Any confirmed or suspected immunosuppression or immunodeficiency condition known from medical history, including human immunodeficiency virus (HIV) infection, asplenia.*
6. *Serious or uncontrolled cardiovascular diseases, nervous system disorders (e.g., Guillain-Barre syndrome), blood and lymphatic system disorders, immune system disorders, hepatorenal disorders, respiratory system disorders (e.g., active tuberculosis, pulmonary fibrosis), metabolic and skeletal systems disorders or malignant tumors (except for skin basal cell carcinoma or in situ carcinoma of uterine cervix that has been cured for more than 5 years).*
7. *Hereditary hemorrhagic tendency or coagulation dysfunction, or a history of thrombosis or hemorrhagic disease, or requirement of continuous use of anticoagulants.*
8. *Prior use of any medication to prevent COVID-19 within 1 week before signing the informed consent form (except for previous vaccines, BBIBP-CorV or CoronaVac), e.g, use of antipyretics without pyrexia and any other symptoms.*
9. *Received attenuated live vaccine within 28 days before the vaccination or any other vaccines (licensed or investigational) within 14 days before the vaccination. *
10. *Has participated in an interventional clinical study within 1 months prior to the day of vaccination.*
11. *Injection of immunoglobulin and/or other blood products within 3 months before the administration of study vaccine.*
12. *Long-term use (continuous use > 14 days) of glucocorticoids (≥ 10 mg/day of prednisone or its equivalent dose) or other immunosuppressive agents within 6 months before signing the informed consent form; however, enrollment is allowed for the following conditions: inhaled or topical use of topical steroids, or short-term use (treatment course ≤ 14 days) of oral steroids.*
13. *Pregnant or breastfeeding women.*
14. *Planning to donate blood during the study period.*
15. *Suspected or known alcohol or drug dependence.*

16. *History of severe psychiatric disorders which may affect study participation.*
17. *Planning to permanently move from the local area before study completion or leave the local area for a long time during the period of study visits, so that the scheduled visits cannot be followed.*
18. *Those considered by the investigator as inappropriate to participate in the study.*

11. Luaran Uji Klinik/*Endpoint* : *Luaran Primer / Primary Endpoints:*

Efficacy

Relative vaccine efficacy of V-01 as a booster to prevent the first occurrence of symptomatic and RT-PCR positive COVID-19 (mild or above severity) starting from more than 14 days after the administration of investigational product (≥ 15 days)

Safety

The incidence of AEs within 28 days after the administration of investigational product, including solicited AEs within 7 days and unsolicited AEs within 28 days after the administration of investigational product.

Luaran Sekunder / Secondary endpoints

Efficacy

1. *Relative vaccine efficacy of V-01 as a booster to prevent the first occurrence of severe or above COVID-19 starting from more than 14 days after the administration of investigational product (≥ 15 days)*
2. *Relative vaccine efficacy of V-01 as a booster to prevent symptomatic and RT-PCR positive COVID-19 (mild or above severity) starting from more than 14 days after the administration of investigational product (≥ 15 days) in different age groups, where symptomatic COVID-19 is defined as the primary efficacy endpoint.*
3. *Relative vaccine efficacy of V-01 as a booster to prevent suspected but not confirmed COVID-19 starting from more than 14 days after the administration of investigational product (≥ 15 days),*
4. *Relative vaccine efficacy of V-01 as a booster to prevent death due to a cause attributed to COVID-19 starting from more than 14 days after the administration of investigational product (≥ 15 days).*
5. *Relative vaccine efficacy of V-01 as a booster to prevent hospitalization due to a cause attributed to COVID-19 starting from more than 14 days after the administration of investigational product (≥ 15 days).*
   Note: hospitalization refers to the need for hospitalization for treatment/observation due to the severity of COVID-19 based on the judgement of the investigator, and does not include hospitalization due to local policy reasons (for example, being isolated in hospital due to the positive SARS-CoV-2 test result).

Safety

The incidence of SAEs and AESIs within 12 months after the administration of investigational product.

Immunogenicity (immunology subgroup only):

1. *The serum neutralizing antibody geometric mean titers (GMTs) of V-01 and placebo against SARS-CoV-2 wild type prior to the booster dose and on day 14, day 28, day 90, day 180, and day 365 after the administration of investigational product.*
2. *The serum neutralizing antibody geometric mean titers (GMTs) of V-01 and placebo against SARS-CoV-2 variant Delta (B.1.617.2) prior to the booster dose and on day 14 or day 28 after the administration of investigational product in the first 200 participants in immunogenicity subgroup.*

Exploratory:

1. *Genotype analysis of SARS-CoV-2 nucleic acid sequence in symptomatic and RT-PCR-positive COVID-19 cases*
2. *GMT of neutralizing antibody against SARS-CoV-2 variant (at least one current or newly emerging variant in immunogenic samples from at least one immunogenic sample collection time point, 15~50 participants).*

Hasil Evaluasi

Badan POM telah melakukan evaluasi terhadap protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal tanggal 7 Desember 2021 dengan hasil sebagai berikut:

1. Uji klinik fase III primer Vaksin Rekombinan Protein Fusi SARS-CoV-2 (V01) direncanakan dilaksanakan paralel dengan uji klinik booster dengan menggunakan dosis yang sama yaitu 10 mcg. Hal ini berarti, uji klinik vaksin booster dilakukan tanpa menunggu data efikasi vaksin primer. Saat ini belum ada pedoman yang secara jelas mengatur uji klinik vaksin booster dan vaksin yang sudah disetujui untuk booster telah memiliki vaksin efikasi.
2. Kepada pendaftar disampaikan surat penolakan dan uji klinik vaksin sebagai booster dapat diajukan setelah diperoleh data efikasi sebagai vaksin primer.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas ditolak melalui Surat Penolakan No. B-RG.01.06.32.323.12.21.659 tanggal 28 Desember 2021