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

Informasi Umum

1. Uji klinik yang diajukan adalah uji klinik fase III Vaksin Rekombinan Protein Fusi SARS-COV-2 (V01) yang dikembangkan oleh pengembang Livzon Mabpharm, Inc Cina. Vaksin denga platform protein subunit ini telah terdaftar *pada WHO Landscape of Candidate Vaccine.*
2. Uji klinik fase I (mulai Februari 2021) dan fase II (mulai Maret 2021) dilakukan di Cina dan saat ini masih dalam tahap pengamatan hingga 1 tahun. Sebagai data pendukung uji klinik fase III tersedia laporan interim hasil uji klinik fase 1 dan 2 untuk data keamanan dan imunogenisitas 30 hari setelah vaksinasi.

Informasi Uji Klinik

1.	Judul Protokol	:	***Global, Multi-center, Randomized, Double-Blind, Placebo-Controlled, Phase III Clinical Study to Evaluate the Protective Efficacy, Safety, and Immunogenicity of Recombinant SARS-CoV-2 Fusion Protein Vaccine (V-01) in Adults Aged 18 Years and Older*** TG2101V01 Versi 2.0 tanggal 14 Juni 2021
2.	Produk Uji	:	Vaksin Rekombinan Protein Fusi SARS-COV-2 (V-01) 10 mcg diberikan 2 kali secara intramuskular
3.	Produk Pembanding	:	Placebo diberikan 2 kali secara intramuskular
4.	Center / Peneliti	:	1. Pusat Riset Pengelolaan dan Pengendalian Penyakit Infeksi Direktorat Riset dan Pengabdian Masyarakat, Universitas Padjadjaran / DR. Dr. Bachti Alisjahbana, SpPD(K)PTI, MD, PhD. 2. Rumah Sakit Universitas Andalas / Dr. Russilawati, SpP(K) 3. Fakultas Kedokteran Universitas Udayana / DR. Dr. I Made Susila Utama, SpPD-KPTI FINASIM 4. Fakultas Kedokteran Universitas Islam Negeri Syarif Hidayatullah / Dr. Hari Hendarto, PhD, SpPD-KEMD, FINASIM 5. Fakultas Kedokteran Universitas Indonesia / DR. Dr. Erni Juwita Nelwan, SpPD, KPTI, FACP-FINASIM, PhD 6. Fakultas Kedokteran Universitas Mulawarman / Dr. dr. Carta Agrawanto Gunawan, Sp.PD-KPTI, FINASIM
5.	Sponsor / ORK	:	Livzon Mabpharm Inc. China / PT. Equilab International
6.	Persetujuan Etik	:	1. No. KET-860/UN2.F1/ETIK/PPM.00.02/2021 tanggal 6 September 2021 dari Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Indonesia – RSUPN Dr. Cipto Mangunkusumo. 2. No. 736/UN6.KEP/EC/2021 tanggal 3 September 2021 dari Komisi Etik Penelitian Universitas Padjadjaran Bandung. 3. No. B-012/F12/KEPK/TL.00/8/2021 tanggal 19 Agustus 2021 dari Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Islam Negeri Syarif Hidayatullah Jakarta.

Dirilis oleh BPOM 19 Oktober 2021

4. No. 2313/UN14.2.2.VII.14/LT/2021 tanggal 6 September 2021 dari Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Udayana.
5. No. 79/KEPK-FK/IX/2021 tanggal 17 September 2021 dari Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Mulawarman Samarinda.

7. Desain Uji Klinik : *Global, multicenter, randomized, double-blind, placebo-controlled, parallel-group phase III clinical study.*Jumlah
8. Jumlah Subjek : *22.500 subjects*

9. Tujuan Uji Klinik :

a. *Primary Objective*

Efficacy: To evaluate the efficacy of the recombinant SARS-CoV-2 fusion protein vaccine (V-01) for the prevention of symptomatic RT-PCR-positive COVID-19 (mild or above severity) starting from at least 14 days (≥15 days) after full-course immunization (completing all vaccinations);

Safety: To evaluate the incidence of adverse events (AEs) of recombinant SARS-CoV-2 fusion protein vaccine (V-01) from the first vaccination to 28 days after full-course immunization;

b. *Secondary Objectives:*

Efficacy:

- *To evaluate the efficacy of the recombinant SARS-CoV-2 fusion protein vaccine (V-01) for the prevention of COVID-19 of severe or above severity starting from at least 14 days (≥15 days) after full-course immunization*
- *To evaluate the efficacy of the recombinant SARS-CoV-2 fusion protein vaccine (V-01) for the prevention of symptomatic RT-PCR-positive COVID-19 (mild or above severity) starting from at least 14 days (≥15 days) after the first vaccination;*
- *To evaluate the efficacy of the recombinant SARS-CoV-2 fusion protein vaccine (V-01) for the prevention of symptomatic RT-PCR-positive COVID-19 (mild or above severity) starting from at least 14 days (≥15 days) after full-course immunization in different age groups;*
- *To evaluate the morbidity of suspected but not confirmed COVID-19 (negative or not detected);*
- *To evaluate the mortality caused by COVID-19;*
- *To evaluate the hospitalization rate caused by COVID-19;*

Safety

To evaluate the incidence of serious adverse events (SAEs) and adverse events of special interest (AESIs) occurred from the first dose of recombinant SARS-CoV-2 fusion protein vaccine (V-01) to 12 months after full-course immunization;

Immunogenicity (immunology subgroup only):

- *To evaluate the seroconversion rate of serum SARS-CoV-2 RBD protein-binding antibody, geometric mean titer (GMT) and geometric mean increase (GMI) at day 28, month 3, month 6,*

and month 12 after full-course immunization (enzyme-linked immunosorbent assay [ELISA]);

- *To evaluate the seroconversion rate of serum anti-SARS-CoV-2 neutralizing antibody, GMT and GMI at day 28, month 3, month 6, and month 12 after full-course immunization (live virus neutralization assay);*

Exploratory objectives:

- *To evaluate the severity of COVID-19 of participants in the vaccine group versus the control group, so as to evaluate the vaccine-mediated antibody-dependent enhancement (ADE);*
- *To explore the correlation of immunogenicity and efficacy through evaluating the titer level of RBD protein-binding antibody in confirmed COVID-19 cases.*
- *Genotypic analyses of SARS-CoV-2 nucleic acid sequence in symptomatic and RT-PCR-positive COVID-19 cases.*

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

1. *Voluntarily participate in this study and sign the informed consent form;*
2. *Adults aged 18 years and older, male or female;*
3. *According to the assessment of the investigator, the participant has a stable medical condition (which is defined as no significant changes in therapy or hospitalization caused by disease aggravation within 3 months before enrollment) and is able to and willing to follow the requirements of the protocol.*
4. *Males of reproductive potential and females of child-bearing potential voluntarily agree to take effective and acceptable contraceptive methods from the signing of informed consent form to 12 months after full-course immunization; females of child-bearing potential have a negative pregnancy test at screening and at the day of vaccination.*

Kriteria Eksklusi / *Exclusion criteria*

1. *History of previous COVID-19 infection;*
2. *Positive result for RT-PCR test in the screening period or specific antibody IgG or IgM meet the following criteria:*
   a. *If IgG is positive, the participant will be excluded regardless of the results of other indexes.*
   b. *If IgG is negative and IgM is positive, it will be determined whether or not to enroll such participant after the result of RT-PCR test is obtained;*
   c. *If both IgG and IgM are negative, the participant can be vaccinated without waiting for the RT-PCR test results.*
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 medications to prevent COVID-19, e.g., use of antipyretics without pyrexia and any other symptoms;*
9. *A history of vaccination against SARS-CoV-2 (marketed or investigational);*
10. *Received attenuated live vaccine within 28 days before the first vaccination or any other vaccines (licensed or investigational) within 14 days before the first 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 (≥10mg/day of prednisone or its equivalent dose) or other immunosuppressive agents; 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

The efficacy of V-01 for the prevention of symptomatic RT-PCR- positive COVID-19 (mild or above severity) starting from at least 14 days (≥15 days) after full-course immunization;

Safety

The incidence of AEs from the first dose of V-01 to 28 days after full-course immunization;

Immunogenicity

The seroconversion rate of serum SARS-CoV-2 RBD protein-binding antibody, GMT and GMI at day 28, month 3, month 6, and month 12 after full-course immunization; • The seroconversion rate of serum anti-SARS-CoV-2 live virus-neutralizing antibody, GMT and GMI at day 28, month 3, month 6, and month 12 after full-course immunization.

Luaran Sekunder **/** *Secondary endpoints*

Efficacy

- *The efficacy of V-01 for the prevention of COVID-19 of severe or above severity starting from at least 14 days (≥15 days) after full-course immunization;*
- *The efficacy of V-01 for the prevention of symptomatic RT-PCR-positive COVID-19 (mild or above severity) starting from at least 14 days (≥15 days) after the first dose;*
- *The efficacy of V-01 for the prevention of symptomatic RT-PCR-positive COVID-19 (mild or above severity) starting from at least 14 days (≥15 days) after full-course immunization in different age groups;*
- *The morbidity of suspected but not confirmed COVID-19 (negative or not detected);*
- *The mortality caused by COVID-19; • The hospitalization rate caused by COVID-19.*

Safety

The incidence of SAEs and AESIs from the first dose of V-01 to 12 months after full-course immunization.

Hasil Evaluasi

Badan POM telah melakukan evaluasi terhadap protokol yang diajukan yang didukung oleh tim ahli melalui rapat pada tanggal tanggal 6 Juli 2021 dengan hasil sebagai berikut:

1. Data analisis interim uji klinik fase 1 dan 2 menunjukkan vaksin cukup aman dan tidak ditemukan efek samping serius serta kasus kematian. Imunogenisitas vaksin cukup baik, data 28 hari setelah vaksinasi menunjukkan *seroconversion rate* antibodi netralisasi dan *Receptor Binding Domain (RBD)* di atas 95% dan nilai GMT antibodi netralisasi naik hingga 23 kali.
2. Desain uji klinik yang diajukan dapat diterima.
3. Vaksin memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik No. RG.01.06.1.3.10.21.95 tanggal 19 Oktober 2021