RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN SARS-COV-2 MRNA VARIAN DELTA DAN OMICRON
PRODUKSI SUZHOU ABOGEN BIOSCIENCES CO., LTD.

Informasi Umum

1. Uji klinik yang diajukan adalah uji klinik fase I vaksin SARS-CoV-2 Variant mRNA Vaccine untuk varian Omicron (ABO1009-DP) dan Delta (ABO-CoV.617.2) yang dikembangkan oleh Suzhou Abogen Biosciences Co., Ltd., China.
2. Vaksin uji klinik tersebut merupakan vaksin mRNA hasil modifikasi vaksin ARCoV, yang dikembangkan oleh Yuxi Walvax Biotechnology Co., Ltd; Walvax Biotechnology Co., Ltd; dan Suzhou Abogen Biosciences Co., Ltd, China, pada sequence basa mRNA untuk meningkatkan sensitivitas vaksin terhadap virus varian Omicron (vaksin ABO-CoV-617.2) dan Delta (vaksin ABO1009-DP).
3. Uji non klinik telah dilakukan pada *mice* dan *cynomolgus monkeys* untuk mengetahui keamanan dan imunogenisitas vaksin.

Informasi Uji Klinik

1.	Judul Protokol	:	***A Randomized, Double-Blind, and Placebo-Controlled Phase 1 Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of SARS-CoV-2 Variant mRNA Vaccines (ABO1009-DP and ABO-CoV.617.2) in Indonesian Subjects Aged 18 Years and Older Who Have Not Received SARS-CoV-2 Vaccines*** *Protocol No. ABO1009-CoV.617.2-101-Indonesia versi 2.0 tanggal 23 Mei 2022*
2.	Produk Uji	:	*Modified vaccine based on SARS-CoV-2 mRNA vaccine (ARCoV) consist of:* *a. SARS-CoV-2 variant Omicron mRNA vaccine (ABO1009-DP) consist of 15 µg /0,5 ml* *b. SARS-CoV-2 variant Delta mRNA vaccine (ABO-CoV.617.2) consist of 15 µg/ 0,5 ml.* Vaksin diberikan 2 kali pada hari ke-0 dan 28 secara intramuskular. Produksi: Suzhou Abogen Biosciences Co., Ltd., China.
3.	Produk Pembanding	:	Plasebo (*Normal saline injection*), diberikan 2 kali pada hari ke-0 dan 28 secara intramuskular. Produksi: Suzhou Abogen Biosciences Co., Ltd., China
4.	Center / Peneliti	:	a. RSUP Persahabatan, Jakarta / Dr. dr. Fathiyah Isbaniah, Sp. P(K), MPd, Ked b. RSUPN Dr. Cipto Mangunkusumo, Jakarta / dr. Sukamto Koesnoe, Sp.PD-KAI
5.	Sponsor / ORK	:	Suzhou Abogen Biosciences Co., Ltd. China dan PT. Etana Biotechnologies Indonesia / PT. Tigermed Consulting Indonesia

6. Persetujuan Etik : No. 20.A.2/KEPK-RSUPP/05/2022 tanggal 25 Mei 2022 dari Komite Etik Penelitian Kesehatan Rumah Sakit Persahabatan

7. Desain Uji Klinik : *Study is a randomized, double-blind, placebo-controlled, phase I clinical study to evaluate the safety, tolerability, and immunogenicity of 2 investigational vaccines in the population aged 18 years and older who have not received any vaccines against SARS-CoV-2.*

8. Jumlah Subjek : 60 subjek, dibagi menjadi kelompok ABO1009-DP, ABO-CoV.617.2, dan plasebo.

9. Tujuan Uji Klinik : *Primary objective*

1. *To evaluate the safety and tolerability of ABO1009-DP administered in 2 doses with an interval of 28 days*
2. *To evaluate the safety and tolerability of ABO-CoV.617.2 administered in 2 doses with an interval of 28 days.*

Secondary objectives

1. *To evaluate the immunogenicity of ABO1009-DP against SARS-CoV-2 (original strain, Delta variant and Omicron variant)*
2. *To evaluate the immunogenicity of ABO-CoV.617.2 against SARS-CoV-2 (original strain, Delta variant and Omicron variant)*
3. *To evaluate the long-term safety of ABO1009-DP*
4. *To evaluate the long-term safety of ABO-CoV.617.2*

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

1. *Voluntarily sign the ICF approved by the Ethics Committee before any study procedure and agree to participate in the study.*
2. *Healthy male or female able to provide legal identity certificate and aged 18 years and older when signing the ICF.*
3. *Have not previously received any SARS-CoV-2 vaccine (marketed or investigational) before screening.*
4. *Be able to communicate well with the investigator, and to understand and comply with the requirements of this clinical trial.*
5. *Males or females of childbearing potential voluntarily take effective contraceptive methods from signing ICF to 3 months after the last vaccination, including sexual abstinence or effective contraceptive measures (e.g., intrauterine or implanted contraceptive device, oral contraceptives, injected or implanted contraceptives, sustained-release topical contraceptives, intrauterine device [IUD], condoms [male], diaphragm, and cervical cap).*

Kriteria Eksklusi / *Exclusion criteria*

1. *Subjects who do not meet health standard upon comprehensive physical examination, mainly including:*
   a. *Abnormal vital signs (pulse < 60 bpm or > 100 bpm, systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg when keeping awake) with clinical significance.*
   b. *Body mass index (BMI) < 18 kg/m2 or > 30 kg/m2.*

c. *Abnormal laboratory values and with clinical significance at the investigator's discretion at screening.*
d. *Subjects who do not remain overall healthy (i.e., is anticipated to have fatal outcome of uncontrolled diseases within 12 months and is not able to provide blood as specified by the trial with anticipated, deleterious medical consequences) in the clinical judgment of the investigator based on medical history and physical examination.*

2. *SARS-CoV-2 specific antibody positive at screening.*
3. *Positive SARS-CoV-2 RT-PCR result at screening.*
4. *Prior medical history of SARS-CoV-2, severe acute respiratory syndrome (SARS), middle east respiratory syndrome (MERS), or other human coronavirus infections or diseases.*
5. *Fever (axillary temperature ≥ 37.3℃) on the day of vaccination with this study vaccine or within recent 72 hours.*
6. *Pregnant or lactating women, or those who plan to donate sperm or egg during the trial.*
7. *Prior history of allergic reaction or anaphylaxis to any vaccine or its excipients, e.g., hypersensitivity, urticaria, serious eczema, dyspnea, laryngeal edema, and angioedema etc.*
8. *Prior use of any vaccine within 28 days before using this study vaccine or planning to use any vaccine other than this study vaccine during the study period.*
   Note: The exception is that licensed influenza vaccines can be received more than 28 days after the second dose of study injection.
9. *Participation in the studies of any other interventional device or drug within 30 days before the screening, or current treatment with other investigational drug(s) or within 5 half-lives after taking the last dose of the study drug.*
10. *Hereditary hemorrhagic tendency or coagulation dysfunction (e.g., cytokine defects, coagulation disorders or platelet disorder), or a history of serious bleeding, or a history of massive bleeding after intramuscular injection or intravenous puncture or ecchymosis.*
11. *Known medical history or diagnosis confirming that subjects have diseases affecting immune system function, including cancer (except skin basal cell carcinoma), congenital or acquired immunodeficiency (e.g., infection with human immunodeficiency virus [HIV]), uncontrolled autoimmune disease.*
12. *Serious or uncontrolled respiratory system disorders, cardiovascular disorders, nervous system disorders, blood and lymphatic system disorders, liver and kidney disorders, metabolism and skeletal disorders, etc. influencing study results evaluation at the investigator's discretion.*
13. *Asplenia or functional asplenia.*

14. *Long-term use (continuous use ≥ 14 days) of immunosuppressants or other immunomodulators (e.g., glucocorticoids: prednisone or similar drugs) within 6 months prior to administration of this investigational vaccine, except for topical medications (e.g., ointments, eye drops, inhalants or nasal sprays). And the topical medications should not exceed the recommended dose in the labels for use or induce any signs of systemic exposure.*
15. *Having received immunoglobulins and/or blood products within 3 months prior to administration of this investigational vaccine.*
16. *Suspected or known alcohol dependency or drug abuse, which may affect safety evaluation or subject's compliance at the investigator's discretion.*
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.*
18. *Receiving antituberculosis treatment.*
19. *Staff of test site, sponsor and contract research organization (CRO) taking part in the study.*

Postponement criteria for the second dose

If the subjects have any of the followings prior to the second dose, vaccination will be postponed. During the same immunization schedule, the second dose of vaccine will be administered at the 28th day after the first dose, with a time window of +7 days:

1. *Fever (axillary temperature ≥ 37.3℃, COVID-19 should be excluded) on the day of the second dose or within recent 72 hours.*
2. *In case of any acute disease prior to the second dose, the investigator should exclude COVID-19, and assess that the acute disease can recover in a short term.*
3. *Subjects cannot reach the vaccination site on the day of the second dose due to special situations (including healthy population quarantined due to the epidemic).*

Exclusion Criteria for the second dose

If the subjects have any of the followings prior to the second dose, vaccination will be terminated. However, other study procedures can be continued at the discretion of the investigators:

1. *Positive pregnancy test for female subjects of childbearing potential.*
2. *Positive SARS-CoV-2 RT-PCR result.*
3. *Serious hypersensitivity or serious adverse event causally related to vaccination has occurred following the first dose.*
4. *Other circumstances considered by the investigator as inappropriate to receive the second dose of the vaccine*

11. *L*uaran Uji Klinik/ *Endpoint* :

Primary endpoints

Safety

1. *Solicited adverse events 0 to 7 days after each injection*
2. *Unsolicited adverse events 0 to 28 days after each injection*
3. *Adverse reactions/events related to blood chemistry, blood routine, blood coagulation function and urinalysis indicators 4 days after each injection*

Secondary endpoints

Immunogenicity

1. *Anti-SARS-CoV-2 (original strain, Delta variant, and Omicron variant) S-RBD-specific IgG antibody level, live virus neutralizing titer, and pseudovirus neutralizing titer before the first injection (Day 0), 28 days after the first injection (before the second injection), 14 days, 28 days, 3 months, 6 months, 9 months, and 12 months after 2 injections, and the corresponding ratio against Day 0.*
2. *Seroconversion of anti-SARS-CoV-2 (original strain, Delta variant and Omicron variant) S-RBD-specific IgG antibody, live virus neutralizing antibodies, and pseudovirus neutralizing antibodies 28 days after the first injection (before the second vaccination), 14 days, 28 days, 3 months, 6 months, 9 months, and 12 months after 2 injections.*

   Note: Antibody seroconversion refers to: For the population with antibody titer below the lower limit of quantitation (LLOQ) before vaccination, antibody titer increases to the lower limit of quantitation or above after vaccination. For the population with antibody titer at the lower limit of quantitation or above before vaccination, antibody titer increases at least 4 times after vaccination.
3. *The number of T cells producing cytokines IFN-γ (original strain and Omicron variant) before the first injection (Day 0), 14 days and 6 months after 2 injections in the cellular immunogenicity subgroup.*

Safety

Serious adverse events (SAEs), adverse events of special interest (AESIs), and other medically attended adverse events (MAAEs) through 12 months after 2 injections

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik SARS-CoV-2 Variant mRNA Vaccine untuk varian Omicron (ABO1009-DP) dan Delta (ABO-CoV.617.2), yang didukung oleh tim ahli melalui rapat pada tanggal 28 April 2022 dengan hasil sebagai berikut:

1. Hasil uji non-klinik vaksin uji dan vaksin prototipe untuk mengetahui keamanan dan imunogenisitas vaksin telah dilakukan pada *mice* dan *cynomolgus monkeys* menunjukkan produk yang akan digunakan dalam uji klinik memiliki (i) profil keamanan yang masih dapat ditoleransi dengan baik (ii) imunogenisitas yang baik dan menginduksi imunitas terhadap infeksi SARS-CoV-2 pada hewan model.
2. Untuk memastikan keamanan subjek pada uji klinik fase 1, rekrutmen subjek dilakukan bertahap dan dilakukan evaluasi keamanan terlebih dahulu oleh peneliti dan tim *Data Safety Monitoring Board* (DSMB) pada setiap tahap.
3. Desain uji klinik yang diajukan telah memadai.
4. Vaksin uji klinik yang akan digunakan telah memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik Nomor RG.01.06.1.3.06.22.82 tanggal 2 Juni 2022.