RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN MONOVALENT OMICRON SUBLINEAGE BA.4/BA.5 (ABO1020) PRODUKSI
SUZHOU ABOGEN BIOSCIENCES CO., LTD

Informasi Umum

1. Vaksin AWcorna merupakan vaksin mRNA SARS-COV-2 yang dikembangkan menggunakan **varian Wuhan** oleh Yuxi Walvax Biotechnology Co., Ltd; Walvax Biotechnology Co., Ltd; dan Suzhou Abogen Biosciences Co., Ltd, China. Vaksin tersebut telah mendapatkan persetujuan EUA sebagai vaksin primer dan booster heterolog di Indonesia.
2. Vaksin AWcorna dimodifikasi pada sequence basa mRNA untuk meningkatkan sensitivitas vaksin terhadap virus SARS-COV-2 varian lainnya sebagai berikut:
   a. Vaksin Monovalent untuk varian Omicron BA.1 (**ABO1009-DP)** dan Delta (**ABO-CoV.617.2).** Telah dilakukan uji klinik **fase I** dengan merekrut 60 subjek. Tersedia data keamanan per tanggal 18 November 2022 dengan kesimpulan ABO1009-DP (vaksin terhadap varian Omicron BA.1) dan ABO-CoV.617.2 (vaksin terhadap varian Delta) dinilai aman dan dapat ditoleransi dengan baik.
   b. Vaksin Bivalent (**ABO1015-DP)** yang merupakan kombinasi vaksin monovalent varian Omicron BA.1 dan Delta, tidak dilanjutkan ke tahapan uji klinik.
   c. Vaksin Monovalent Omicron sublineage BA.4/5 (**ABO1020**) saat ini diajukan ke Badan POM untuk uji klinik fase II/ III yang protokolnya merupakan gabungan fase I/ II/ III.

Informasi Uji Klinik

1. Judul protokol : ***A Randomized, Double-blind, Placebo-controlled Clinical Study to Evaluate the Efficacy, Safety, and Immunogenicity of SARSCoV-2 Variant (BA.4/5) mRNA Vaccine (ABO1020) in Healthy Subjects Aged 18 Years and Older Who Have Completed the Full Vaccination***
   Protocol No. ABO1020-301 Protocol Amendment IDN-2.0 dated 28 Nov 2022
2. Produk Uji : Nama: Vaksin SARS-COV-2 variant (BA.4/5) mRNA (ABO1020). Vaksin diberikan 2 (dua) kali pada hari ke-0 dan hari ke-28 secara intramuskular.
   Produsen: Suzhou Abogen Biosciences Co., Ltd, China
3. Produk Pembanding : Nama: placebo. Vaksin diberikan 2 (dua) kali pada hari ke-0 dan hari ke-28 secara intramuskular.
   Produsen: Suzhou Abogen Biosciences Co., Ltd, China
4. Center/ Peneliti : **Center/ Koordinator Peneliti :** Rumah Sakit Umum Pusat Persahabatan, Jakarta/ Dr. dr. Erlina Burhan, MSc, Sp.P(K)

   ***Center* / Peneliti :**

   1. RSUP Persahabatan Jakarta / dr. Raden Rara Diah Handayani, Sp.P(K)
   2. RSUPN Dr. Cipto Mangunkusumo Jakarta / dr. Ceva Wicaksono Pitoyo, SpPD, KP, KIC, FINASIM
   3. RS Universitas Indonesia Depok / dr. Rania Imaniar, Sp.P
   4. RSUD Tarakan Jakarta / dr. Indawati, Sp.P
   5. RSIJ Cempaka Putih Jakarta / dr. Cut Yulia Indah Sari, Sp.P
   6. RS Yarsi Jakarta / dr. Efriadi Ismail, Sp.P
5. Sponsor/ ORK : Suzhou Abogen Biosciences Co., Ltd. China dan PT. Etana Biotechnologies Indonesia / PT. Tigermed Consulting Indonesia

6. Persetujuan Etik :
   1. No. 80/KEPK-RSUPP/09/2022 tanggal 6 September 2022 dan No. 80.A.1/KEPK-RSUPP/12/2022 tanggal 23 Desember 2022 dari Komite Etik Penelitian Kesehatan Rumah Sakit Persahabatan
   2. No. KET-1317/UN2.F1/ETIK/PPM.00.02/2022 tanggal 28 November 2022 dan No. S-857/UN2.F1/ETIK/PPM/00.02/2022 tanggal 26 Desember 2022 dari Komite Etik Penelitian Kesehatan Fakultas Kedokteran Universitas Indonesia – RSUPN Dr. Cipto Mangunkusumo.

7. Desain Uji Klinik : *The Phase 2/3 part is a randomized, double-blind, multi-center and placebo-controlled study to evaluate the efficacy, safety and immunogenicity of 2-dose vaccination of ABO1020 in healthy adults aged 18 years and older who have previously been vaccinated by 2 or 3 doses of SARS-CoV-2 inactivated vaccine.*

8. Jumlah subjek : Total enrolled 15000 subject. Randomized in a ratio 1:1 (ABO1020 Group 7500 subject and Placebo group 7500 subject)

9. Tujuan uji klinik :

Primary objective

Efficacy

To evaluate the efficacy of ABO1020 against confirmed COVID-19 occurring from 14 days after the second dose, as compared to placebo.

Secondary objectives

Efficacy

1. *To evaluate the efficacy of ABO1020 against confirmed COVID-19 occuring from 14 days after the first dose in subjects.*
2. *To evaluate the efficacy of ABO1020 against confirmed COVID-19 after each dose.*
3. *To evaluate the efficacy of ABO1020 against asymptomatic SARS-CoV-2 infection after each dose.*
4. *To evaluate the efficacy of ABO1020 against severe confirmed COVID-19 after each dose.*
5. *To evaluate the efficacy of ABO1020 against different genotype of SARSCoV- 2 virus infection after each dose.*

Immunogenicity

*To evaluate the **humoral immunity** of ABO1020 28 days after each dose, 90 days and 180 days after the second dose in the humoral immunity subgroup*

Safety

1. *To evaluate the safety of ABO1020 within 28 days after each dose in all subjects.*
2. *To evaluate the long-term safety of ABO1020 in all subjects.*

10. Kriteria Eligibilitas :

Inclusion Criteria:

The subjects must meet all of the following 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. *Subjects who have previously been fully vaccinated either by **2 or 3 doses of SARS-CoV-2 inactivated vaccine**. The last dose of immunization should be **>6 months** before administration of the investigational products.*

4. *Be able to communicate well with the investigator, and to understand and comply with the requirements of this clinical trial.*
5. *Males and females with childbearing potential voluntarily take effective contraceptive methods from signing ICF to 3 months after completing the 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).*

Exclusion Criteria

Exclusion criteria for the first dose

Subjects should not participate in this clinical study if any of the following criteria is met before the 1st dose of the investigational product:

1. *Positive SARS-CoV-2 rapid test at screening.*
2. *Prior medical history of severe acute respiratory syndrome (SARS), middle east respiratory syndrome (MERS).*
3. *Fever (axillary temperature or equivalent ≥ 37.3℃*) on the day of vaccination with this investigational vaccine or within recent 72 hours.*
   ** Tympanic Temperature °C – 0.56°C = Axillary Equivalent in °C*
4. *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 relevance.*
5. *Do not remain overall healthy (i.e., has medically deteriorated significantly since receiving the two-dose vaccination, 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.*
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 other vaccine within 28 days before using the investigational products or planning to use any vaccine other than the investigational products during the study period.*
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]), and 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 study site, sponsor and contract research organization (CRO) taking part in the study.*
20. *Other conditions that the investigators consider unsuitable for this study.*

11. Luaran Uji Klinik/ Endpoint :

Primary endpoint
Efficacy
Confirmed COVID-19 cases occurring from 14 days after the second dose.

Secondary endpoints
Efficacy
1. *Confirmed COVID-19 cases occurring from 14 days after the first dose*
2. *Confirmed COVID-19 cases after each dose*
3. *Asymptomatic SARS-CoV-2 infection after each dose*
4. *Severe confirmed COVID-19 cases after each dose*
5. *SARS-CoV-2 genotype of cases having assessable RT-PCR samples after each dose.*

Immunogenicity
Anti-SARS-CoV-2 (Omicron sublineage BA.4/BA.5) ***live virus neutralizing antibody titer****, 28 days after each dose, 90 days and 180 days after the second dose and the corresponding ratio against Day 0 before the vaccination.*

Safety
1. *Solicited AEs 0 to 14 days and unsolicited AEs 0 to 28 days after each dose.*
2. *SAEs and AESIs through 12 months after each dose.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik *Vaksin Monovalent Omicron Sublineage* BA.4/BA.5 (ABO1020) yang didukung oleh tim ahli melalui rapat pada tanggal 19 Desember 2022.

Telah tersedia uji non klinik untuk imunogenisitas (netralisasi antibodi) dan uji tantang pada hewan uji tikus, uji anafilaksis pada *Guinea Pigs*, uji *local muscle irritation* pada rabbit, dan uji toksisitas. Uji klinik fase II untuk dose ranging karena dosis vaksin Monovalent Omicron sublineage BA.4/5 (**ABO1020**) mengikuti Vaksin AWcorna.

Berdasarkan hasil uji non klinik untuk uji imunogenisitas, uji tantang dan uji toksisitas, vaksin dapat ditoleransi dengan baik dan menghasilkan respon imun antibodi (IgG dan netralisasi antibodi) setelah pemberian suntikan pertama dan meningkat pada suntikan kedua. Desain uji klinik yang diajukan telah memadai. 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.01.06.1.3.01.23.04 tanggal 18 Januari 2023