RINGKASAN HASIL EVALUASI PERMOHONAN
PERSETUJUAN PELAKSANAAN UJI KLINIK
VAKSIN AdimrSC-2f PRODUKSI ADIMMUNE CORPORATION
SEBAGAI VAKSIN PRIMER PADA DEWASA

Informasi Umum

1. Vaksin AdimrSC-2f dikembangkan oleh Adimmune Corporation, Taiwan. Vaksin AdimrSC-2f merupakan vaksin COVID-19 dengan *platform* protein rekombinan yang mengandung *Receptor Binding Domain* (RBD) dari protein Spike (S) SARS-CoV-2 yang diproduksi oleh sistem ekspresi vektor baculovirus.
2. Tahapan pengembangan vaksin yaitu: uji nonklinik telah dilakukan pada tikus, hamster dan kelinci untuk mengetahui keamanan dan imunogenisitas vaksin serta uji klinik fase I di Taiwan.

Informasi Uji Klinik

1.	Judul Protokol	:	***A Phase I/II, Placebo-Controlled, Randomized, Double-Blind, Dose-Finding Study to Evaluate The Safety, Tolerability, and Immunogenicity of AdimrSC-2f Vaccine in Healthy Adults*** No. ADPCT21013I Version 1.3 Tanggal 9 Juni 2021
2.	Produk Uji	:	AdimrSC-2f Vaccine (Protein rekombinan RBD dari protein Spike (S) SARS-CoV-2 50 µg & 100 µg dan Al(OH)) diberikan 3 kali secara intramuskular. Produsen: Adimmune Corporation
3.	Produk Pembanding	:	Phosphate Buffered Saline dan Al(OH)3 diberikan 3 kali secara intramuskular. Produsen: Adimmune Corporation
4.	Center / Peneliti	:	Rumah Sakit Akademik Universitas Gadjah Mada, Yogyakarta / dr. Astari Pranindya Sari, M.Sc., Sp.P.
5.	Sponsor / ORK	:	Adimmune Corporation, Taiwan / PT. IQVIA RDS Indonesia
6.	Persetujuan Etik	:	No. KE/FK/0687/EC/2021 tanggal 18 Juni 2021 dari Komisi Etik Penelitian Kedokteran dan Kesehatan Fakultas Kedokteran, Kesehatan Masyarakat dan Keperawatan Universitas Gadjah Mada-RSUP Dr. Sardjito Yogyakarta.
7.	Desain Uji Klinik	:	*This will be a Phase I/II, placebo-controlled, randomized, double-blind within dose cohort, dose-finding study to evaluate the safety, tolerability, and immune response of AdimrSC-2f vaccine against SARS-CoV-2 in healthy adults aged from 18 to 60.* *A sequential enrollment strategy will be applied in this study. The eligible subjects will be sequentially assigned from low dose to high dose cohort. The study will be started at the low dose cohort. The first 4 enrolled subjects will be randomized into A: 50 mcg Antigen with 250 mcg Al(OH)3 or matched PBS plus 250 mcg Al(OH)3 (Placebo) in a ratio of 3:1. When these 4 subjects receives the first dosing and do not have any of the following circumstance within 7 days after the 1st dosing, the next 12 subjects will be enrolled and randomized in a 9:3 ratio.Independent DSMB for the safety and tolerability data review. When the DSMB accepts for the safety profiles, enrollment will continue to recruit.*

8. Jumlah Subjek : *Two hundred forty (240) subjects will be sequentially enrolled from low dose to high dose cohort and then randomized into AdimrSC-2f vaccine group or matched placebo in a 3:1 ratio. The low dose cohort includes Group A: 50 mcg AdimrSC-2f vaccine antigen with 250 mcg aluminum hydroxide as adjuvant and matched PBS plus 250 mcg aluminum hydroxide; the median dose cohort includes Group B: 100 mcg AdimrSC-2f vaccine antigen with 250 mcg aluminum hydroxide and matched PBS plus 250 mcg aluminum hydroxide; the high dose cohort includes Group C: 100 mcg AdimrSC-2f vaccine antigen with 500 mcg aluminum hydroxide and matched PBS plus 250 mcg aluminum hydroxide. The subject ratio of Group A, B, C and D is 1:1:1:1 (60 subjects for each group).*

9. Tujuan Uji Klinik : *To evaluate the safety and immunogenicity of AdimrSC-2f vaccine in healthy adults aged from 18 to 60 years old.*

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

1. *Subjects aged 18 to 60 years old (inclusive) at the time of informed consent who are in good general health in the opinion of the investigator.*
2. *At Screening Visit (V0), subjects with a body mass index (BMI) > 18.5 kg/m2 or ≤ 30.0 kg/m2*
3. *Subjects without known history of SARS-CoV-2 infection or known close contact with anyone with laboratory-confirmed SARS-CoV-2 infection or COVID-19 within 2 weeks prior to the first dosing (V1).*
4. *Subjects are willing and able to give informed consent prior to any screening procedure conducting and to comply with study procedures.*
5. *Female subjects of childbearing potential (defined as any female who has experienced menarche and who is NOT surgically sterile [ie, hysterectomy, bilateral tubal ligation, or bilateral oophorectomy] or postmenopausal [defined as amenorrhea at least 12 consecutive months or documented plasma follicle-stimulating hormone level ≥40 mIU/mL]) must agree to be heterosexually inactive from at least 21 days prior to the Screening Visit (V0) and through 6 months (defined as 24 weeks) after the last dosing OR agree to consistently use any of the following methods of contraception from at least 21 days prior to the Screening Visit (V0) and through 6 months (defined as 24 weeks) after the last dosing:*
   a) *Condoms (male or female) with spermicide (if acceptable in country)*
   b) *Diaphragm with spermicide*
   c) *Cervical cap with spermicide*
   d) *Intrauterine device*
   e) *Oral or patch contraceptives*
   f) *Norplant®, Depo-Provera®, or other in country regulatory-approved contraceptive method that is designed to protect against pregnancy.*

g) *Abstinence, as a form of contraception, is acceptable*

Kriteria Eksklusi / *Exclusion criteria*

1. *Subjects who are investigational site staff member directly involved in the conduct of the trial and their family members, site staff members otherwise supervised by the Investigator, or subjects who are Adimmune employees directly involved in the conduct of the trial.*
2. *Any ongoing severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.*
3. *Subject with positive serology test results for human immunodeficiency virus (HIV), hepatitis C virus (HCV) or hepatitis B virus (HBV) at the Screening Visit (V0).*
4. *Subject with positive test result for COVID-19 antigen rapid test at the Screen Visit (V0) or V1 prior to the 1st dosing.*
5. *Subject with influenza-like illness as defined by any of the following symptoms at the Screening Visit (V0) or before randomization (V1): fever (tympanic temperature ≥ 38°C), dry cough, headache, fatigue, respiratory sputum production (phlegm), dysgeusia, anosmia, shortness of breath, muscle and joint pain, or sore throat.*
6. *Participation in other studies involving investigational drug(s) and/or device(s) within 90 days prior to the Screening Visit (V0) and/or during study participation.*
7. *Subject who has received any investigational coronavirus vaccine or has received any medications intended to prevent COVID-19 or plan simultaneous participation in another interventional study to prevent or treat COVID-19.*
8. *Subject with any following ongoing disease or medical history in medical chart or by verbal confirmation:*
    a. *Diagnosis of malignancy not in remission for the past 3 years except nonmelanoma skin cancer prior to the Screening Visit (V0).*
    b. *Chronic pulmonary disease, asthma or wheezing.*
    c. *Chronic liver disease or suspected active hepatitis.*
    d. *Clinically significant cardiovascular disease such as arrhythmia, coronary artery disease or heart failure.*
    e. *Personal or family history of immune disorders, including SLE (systemic lupus erythematosus), rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, and Type 1 diabetes.*
    f. *Any confirmed or suspected abnormal immune function, immunosuppressive, or immunodeficiency.*
    g. *Personal or family history of Guillain-Barré Syndrome.*
    h. *Bleeding diathesis or condition associated with prolonged bleeding.*
    i. *History of anaphylaxis, urticarial or severe adverse reaction associated with a vaccine or AdimrSC-2f or aluminum.*
    j. *Dermatologic conditions that could affect local solicited adverse event assessment per the investigator's opinion.*
9. *Subject who has any of the following prior medication histories:*

a. *Received any vaccine (live, inactivated, or bacterial) within 30 days prior to the Screening Visit (V0).*
b. *Received any blood/plasma products or immunoglobulin within 90 days prior to the Screening Visit (V0).*
c. *Received any systemic corticosteroids or steroids within 30 days prior to the first dosing (V1). Topical, inhaled/nebulized, intra-articular, or nasal corticosteroid/steroids are permitted.*
d. *Received treatment with immunosuppressive therapy, including cytotoxic agents, immunosupressants or system corticosteroids for organ transplant, cancer, or an autoimmune disease, or planned receipt for disease treatment during study period.*
e. *Used bronchodilator within 90 days prior to the Screening visit (V0).*

10. *Subject with current use or history of chronic smoking (defined as ≥ 1 cigarette per day) in the medical chart or by verbal confirmation within 1 year prior to the Screening Visit (V0).*
11. *Subject with the history of illegal substance use or alcohol abuse in the medical chart or by verbal confirmation within 2 years prior to the Screening Visit (V0).*
12. *Female subject who is pregnant or lactating at the Screening Visit or Visit 1 or plan to be pregnant during the study period.*
13. *Subject who has donated ≥ 250 mL of blood product within 28 days prior to the Screening Visit (V0) or who plans to donate blood products during the study period.*
14. *Subject with levels of creatine phosphokinase outside of the reference range at the Screening Visit (V0).*
15. *Subject who is not suitable to participate in this study as judged by the investigator.*

11. Luaran Uji Klinik :

Primary Endpoints:

Immunogenicity: SARS-CoV-2 neutralizing antibody titers:

1. *Geometric mean titers (GMT) change from the Baseline at Visit 7 (21 days after the 3rd dosing).*
2. *Geometric mean increase (GMI) comparing to the Baseline at Visit 7 (21 days after the 3rd dosing).*
3. *Seroconversion rate (SCR) at Visit 7 (21 days after the 3rd dosing)*

Safety profile of AdimrSC-2f vaccine:

– *Adverse events (AEs):*
  1. *Incidence of solicited local and systemic AEs;*
  2. *Incidence of unsolicited AEs;*
  3. *Incidence of AESI;*
  4. *Incidence of MAAEs;*
  5. *Incidence of SAEs;*
  6. *Incidence of discontinuation from study intervention due to AEs;*
  7. *Incidence of Grades 3 and 4 AEs;*
  8. *Incidence of vaccine-related AEs.*
– *Clinically significant changes in clinical and laboratory evaluations*

Secondary Endpoints:

– *Immune responses:*
  1. *SCR of neutralizing antibody at V1, V3, V5, V7, and V8.*

2. *GMT of neutralizing antibody for SARS-CoV-2 at V1, V3, V5, V7, and V8.*
3. *GMI of neutralizing antibody at V1, V3, V5, V7, and V8.*
4. *GMT of SARS-CoV-2 specific IgG antibody at V1, V3, V5, V7, and V8.*
5. *GMI and SCR of SARS-CoV-2 specific IgG antibody at V1, V3, V5, V7, and V8.*

– *Number of subjects with SARS-CoV-2 infection starting on Visit 7 (21 days after the 3rd dosing).*

Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik fase I/II untuk Vaksin AdimrSC-2f. Hasil evaluasi telah didukung tim ahli melalui rapat pada 21 April dan 9 Juli 2021 dengan hasil sebagai berikut:

1. Hasil uji klinik fase I di Taiwan menunjukkan vaksin dapat ditoleransi dengan baik, namun respon antibodi yang terbentuk setelah pemberian vaksin tidak memadai. Berdasarkan hasil uji klinik tersebut, maka dilakukan reformulasi dan dilakukan studi non klinik kembali dengan dosis vaksin lebih tinggi, penambahan *adjuvant* dan peningkatan frekuensi pemberian yang semula 2 kali menjadi 3 kali.
2. Hasil studi non klinik dengan posologi yang sama dengan uji klinik menunjukkan vaksin dapat ditoleransi dengan baik dan menghasilkan respon imun antibodi setelah pemberian suntikan ketiga.
3. Desain uji klinik yang diajukan telah memadai terutama untuk menjamin keamanan subjek, dilakukan rekrutmen subjek bertahap, dimulai dengan dosis terkecil hingga terbesar dan dilakukan evaluasi keamanan terlebih dahulu oleh *Data Safety Monitoring Board* (DSMB) sebelum dilanjutkan ke tahap berikutnya untuk merekrut subjek. Selain itu, untuk subjek yang menerima plasebo akan diberikan vaksin COVID-19 yang telah memperoleh izin edar dari Badan POM setelah studi selesai.
4. Vaksin uji yang akan digunakan telah memenuhi persyaratan mutu.

Keputusan

Pelaksanaan uji klinik dengan protokol di atas disetujui melalui penerbitan Persetujuan Pelaksanaan Uji Klinik No. RG.01.06.1.2.09.21.80 tanggal 8 September 2021.