RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
COVID-19 VACCINE ASTRAZENECA (CHADOX1-S), PFIZER-BIONTECH (COMIRNATY)
DAN *INACTIVATED SARS-COV-2 VACCINE SINOVAC (CORONAVAC®)* SEBAGAI VAKSIN *BOOSTER*

Informasi Umum

1. Badan Penelitian dan Pengembangan Kesehatan, Kementerian Kesehatan RI mengajukan persetujuan uji klinik vaksin booster menggunakan 3 jenis vaksin yang telah mendapatkan Emergency Use Authorization (EUA) sebagai vaksin primer yaitu COVID-19 Vaccine AstraZeneca (ChAdOx1-S), Pfizer-BioNTech (Comirnaty) dan *Inactivated* SARS-CoV-2 Vaccine *(CoronaVac®)* dengan dosis penuh dan setengah dosis pada 1500 subjek yang dikelompokkan menjadi 15 kelompok.
2. Vaksin uji klinik akan diberikan sebagai vaksin *booster* pada subjek yang telah mendapatkan vaksin primer secara lengkap yaitu COVID-19 Vaccine AstraZeneca (ChAdOx1-S) dan Inactivated SARS-CoV-2 Vaccine *(CoronaVac®)* sehingga subjek akan mendapatkan vaksin booster yang homolog atau heterolog.
3. Vaksin uji yang digunakan belum mendapatkan EUA sebagai vaksin *booster* di Indonesia dan baru vaksin Pfizer mendapatkan EUA dari US FDA sebagai vaksin *booster*.

Informasi Uji Klinik

1. Judul protokol : ***Immunogenicity and Safety Study of Half and Full Dose of Heterologous and Homologous COVID-19 Vaccine Booster in Adult Subjects in Indonesia***
   Version 2 dated 15 November 2021
2. Produk Uji :
   a. *COVID-19 Vaccine AstraZeneca (ChAdOx1-S)* produksi *Astra Zeneca*
   b. *Comirnaty Vaccine* produksi *BioNTech Manufacturing GmbH*
   c. *Inactivated SARS-CoV-2 Vaccine (CoronaVac®)* produksi *Sinovac Biotech*

   Vaksin *booster* diberikan 1 (satu) kali secara intravena.
3. Center/Peneliti : Peneliti Utama: Dr. Eddy Fadlyana, dr., Sp.A(K)., MKes

   Center/ Peneliti:
   1. FK Universitas Padjajaran Bandung/ Dr. Djatnika Setiabudi, dr., SpA(K)
   2. FK Universitas Indonesia Jakarta/ dr. Nina Dwi Putri, Sp.A(K)
4. Sponsor : Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan Republik Indonesia
5. Persetujuan Etik : No. LB.02.01/2/KE.672/2021 tanggal 1 November 2021 dari Komisi Etik Penelitian Kesehatan Badan Penelitian dan Pengembangan Kesehatan (KEPK-BPPK) Kementerian Kesehatan Republik Indonesia
6. Desain Uji Klinik : *Observer-blind, randomised controlled trial*
7. Jumlah subjek : 1500 subjek dibagi dalam 15 kelompok
   The subject will be assigned into one of below arms:
   1. *Subjects with CoronaVac® as COVID-19 vaccine primary dose and second dose within **3–<6 months** prior to booster dose, will be randomized to 5 groups to receive either one booster dose of:*
      a. *Comirnaty® (Pfizer Vaccine) 0.3 ml intramuscularly*
      b. *Comirnaty® (Pfizer Vaccine) 0.15 ml intramuscularly*
      c. *ChAdOx1-S (AstraZeneca Vaccine) 0.5 ml intramuscularly*
      d. *ChAdOx1-S (AstraZeneca Vaccine) 0.25 ml intramuscularly*
      e. *CoronaVac® (Sinovac Vaccine) 0.5 ml intramuscularly*

2. *Subjects with CoronaVac® as COVID-19 vaccine primary dose and second dose within **6–9 months** prior to booster dose, will be randomized to 5 groups to receive either one booster dose of:*
   a. *Comirnaty® (Pfizer Vaccine) 0.3 ml intramuscularly*
   b. *Comirnaty® (Pfizer Vaccine) 0.15 ml intramuscularly*
   c. *ChAdOx1-S (AstraZeneca Vaccine) 0.5 ml intramuscularly*
   d. *ChAdOx1-S (AstraZeneca Vaccine) 0.25 ml intramuscularly*
   e. *CoronaVac® (Sinovac Vaccine) 0.5 ml intramuscularly*

3. *Subjects with ChAdOx1-S (COVID-19 Vaccine AstraZeneca) as COVID-19 vaccine primary dose and second dose within 6–9 months prior to booster dose, will be randomized to 5 groups to receive either:*
   a. *Comirnaty® (Pfizer Vaccine) 0.3 ml intramuscularly*
   b. *Comirnaty® (Pfizer Vaccine) 0.15 ml intramuscularly*
   c. *ChAdOx1-S (AstraZeneca Vaccine) 0.5 ml intramuscularly*
   d. *ChAdOx1-S (AstraZeneca Vaccine) 0.25 ml intramuscularly*
   e. *CoronaVac® (Sinovac Vaccine) 0.5 ml intramuscularly*

8. Tujuan uji klinik : ***Primary objective***

To evaluate the antibody titres before and one month (+7 days) after booster dose with full and half booster dose of ChAdOx1-S, Comirnaty®, or CoronaVac®.

Secondary objective

1. *To evaluate the rate and severity of the reactogenicity within 24h, one week and one month of each booster vaccine group*
2. *To compare the immune responses between full and half booster doses of each vaccine studied.*

9. Kriteria Eligibilitas : *Inclusion Criteria:*

1. *Clinically healthy adults aged above 18 years who had completed the primary series of SARS-CoV-2 vaccine with CoronaVac® within 3 to <6 months or 6–9 months prior enrolment to the study or with ChAdOx1-S within 6–9 months prior enrolment to the study.*
2. *Signed written informed consent form and willing to commit to comply with the instructions of the investigator and the schedule of the trial.*

Exclusion Criteria

1. *Those who have already received a third dose of SARS-CoV-2 vaccine*
2. *Concomitantly enrolled or scheduled to be enrolled in another trial.*
3. *Those with fever (temperature > 37.5℃, measured with infrared thermometer/thermal gun), upper respiratory tract infection symptoms such as sneezing, nasal congestion, runny nose, cough, sore throat, loss of taste chills and shortness of breath within 72 hours before enrolment.*
4. *Blood pressure > 180/110 mmHg.*
5. *History of laboratory confirmed COVID-19 within one month prior to study enrolment.*
6. *History of allergy to vaccines or vaccine ingredients, and severe adverse reactions to vaccines, such as urticaria, dyspnea, and angioneurotic edema.*
7. *Those with uncontrolled autoimmune disease such as lupus.*
8. *History of uncontrolled coagulopathy or blood disorders, immune deficiency, and received blood derived product/transfusion within 3 months prior to enrolment.*

9. *Those who received immunosuppressant therapy such as corticosteroid and cancer chemotherapy*
10. *Those with uncontrolled chronic disease, such as severe heart disease, asthma exacerbation*
11. *Subjects who have history of uncontrolled epilepsy (within the last 2 years) or other progressive neurological disorders, such as Guillain-Barre Syndrome*
12. *Those who receive any vaccination within 1 month before and after booster with study vaccine.*
13. *Pregnant woman with ≤13 weeks of pregnancy or pregnancy with sign of preeclampsia (swollen legs, headache, heartburn, blurred vision, blood pressure > 140/90 mmHg).*
14. *Those aged ≥60 years old with difficulty in climbing 10 steps of stairs, frequently experiencing fatigue, difficulty in walking 100–200 m, or having at least 5 comorbidities (hypertension, diabetes, cancer, chronic lung disease, heart attack, congestive heart failure, chest pain, asthma, joint pain, stroke, and kidney disease).*

10. Luaran Uji Klinik/ Endpoint : *Primary Evaluation Criteria*
    1. *Seropositive rate, seroconversion and GMT of SARS-CoV-2 antibody titer at 28 days after booster dose vaccination.*
    2. *Seropositive rate, seroconversion and GMT of neutralizing antibodies at 28 days after booster dose vaccination.*

    Secondary Evaluation Criteria
    Reactogenicity:
    1. *Incidence rate and intensity of solicited and unsolicited adverse events within 24 hours after booster dose vaccination.*
    2. *Incidence rate and intensity of adverse events within 7 days after booster dose vaccination.*
    3. *Incidence rate of and intensity of adverse events within 28 days after booster dose vaccination.*

    Immunogenicity:
    1. *Seropositive rate, GMT of of SARS-CoV-2 antibody titer prior to booster administration of SARS-CoV-2 vaccine.*
    2. *Seropositive rate, GMT of neutralizing antibodies prior to booster administration of SARS-CoV-2 vaccine.*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik *COVID-19 Vaccine Astrazeneca (Chadox1-S), Pfizer-Biontech (Comirnaty)* Dan *Inactivated SARS-CoV-2 Vaccine Sinovac (Coronavac®)* yang didukung oleh tim ahli melalui rapat pada tanggal 10 November 2021. Referensi yang mendukung penggunaan setengah dosis adalah:

a. Uji klinik di Thailand dengan menggunakan dosis penuh dan setengan dosis dari vaksin Corminaty dan Sinovac sebagai *booster* yang memberikan hasil yang sama antara dosis penuh dan setengah dosis.
b. Uji klinik di Inggris dengan menggunakan vaksin Corminaty dosis penuh dan setengah dosis memberikan hasil yang sama antara dosis penuh dan setengah dosis.

Terdapat kebutuhan data dan informasi respon imun subjek apabila dosis vaksin COVID-19 yang telah mendapatkan EUA diberikan sebagai booster dengan setengah dosis sebagai bahan pertimbangan kebijakan pemerintah dalam vaksinasi nasional untuk mencegah penularan COVID-19.

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.01.06.1.3.11.21.61 tanggal 17 November 2021.