RINGKASAN HASIL EVALUASI
PERMOHONAN PERSETUJUAN PELAKSANAAN UJI KLINIK
***GROUP ACYW135 MENINGOCOCCAL CONJUGATE VACCINE (CRM197)* PRODUKSI CANSINO BIOLOGICS**

Informasi Umum

1. Vaksin *Group ACYW135* (CRM197) merupakan vaksin *quadrivalent meningococcal conjugate* yang dikembangkan oleh *CanSino Biologics Inc. Tianjin China* dan pada uji klinik ini bekerja sama dengan PT Etana Biotechnologies Indonesia.
2. Vaksin CRM197 telah mendapatkan izin edar di China untuk anak usia 3 bulan – 3 tahun.
3. Uji klinik fase III yang diajukan mengikutsertakan 1480 subjek dewasa usia 18 - 55 tahun. Pengajuan uji klinik ini didukung dengan uji klinik fase I usia ≥18 tahun.

Informasi Uji Klinik

1.	Judul protokol	:	***A multicenter, randomized, double-blinded, positive controlled phase Ⅲ clinical trial to evaluate lot-to-lot consistency, immunogenicity and safety of Group ACYW135 Meningococcal Conjugate Vaccine (CRM197) in adults aged 18 to 55 years*** *Protocol No.: CTP-MCVF-006 version 1.1 date 12th October 2023*
2.	Produk Uji	:	*Group ACYW135 Meningococcal Conjugate Vaccine (CRM197) yang diberikan 1 (satu) kali secara intramuskular* *Produsen : CanSino Biologics Inc. Tianjin China*
3.	Produk Pembanding	:	*Menactra [Meningococcal (Groups A, C, Y, and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] yang diberikan 1 (satu) kali secara intramuskular* Produsen : Sanofi Pasteur Biological Products Co. Ltd.
4.	Center/Peneliti		Koordinator Peneliti: Prof. Dr. dr. Erni Juwita Nelwan, PhD, SpPD, K-PTI 1. Rumah Sakit Universitas Airlangga Surabaya/ Prof. Dr. dr. Nasronudin, Sp.PD-KPTI, FINASIM 2. Rumah Sakit Husada Utama Surabaya/ dr. Isti Suharjanti, Sp.S(K)
5.	Sponsor/ ORK	:	CanSino Biologics Inc. China dan PT Etana Biotechnologies Indonesia/ PT. Tigermed Consulting Indonesia
6.	Persetujuan Etik	:	No. 102/KEP/2023 tanggal 7 Juli 2023 dari Komite Etik Penelitian Rumah Sakit Universitas Airlangga untuk kedua center uji klinik.
7.	Desain Uji Klinik	:	*Randomized, observer blinded, active controlled, multicenter clinical study*
8.	Jumlah subjek	:	1480 subjek sehat usia 18 – 55 tahun.
9.	Tujuan uji klinik	:	***Primary Objectives****:* *1. To evaluate the lot-to-lot consistency for 3 lots of Group ACYW135 Meningococcal Conjugate Vaccine (CRM197) (MCV4) administered in single dose immunization schedule, with respect to its immunogenicity* *2. To demonstrate that the immune response induced by a single dose of MCV4 is noninferior to the immune response induced by a single dose of Menactra, in ACYW135 vaccine-naïve subjects only. Immune response shall be measured by serum bactericidal activity assays with rabbit complement (rSBA titre) against serogroup A, C, Y and W135 strains.* *3. To evaluate the safety profile of MCV4 in people aged 18 to 55 years*

***Secondary Objectives**:*

To evaluate the immuno-persistence of MCV4 in people aged 18 to 55 years

10. Kriteria Eligibilitas :

Inclusion Criteria:

1. *Participants aged 18-55 years old at the time of screening, who are in good health condition as determined by the study clinician.*
2. *Participants who have not been vaccinated with any meningococcal vaccines (including but not limited to meningococcal group A and C conjugate vaccine, meningococcal group A and C polysaccharide vaccine, Group ACYW135 Meningococcal polysaccharide/conjugate vaccine);*
3. *The participant or participant's legal guardian signs the informed consent form (ICF) and participant agrees to comply with the requirements of protocol and finish the 1-year follow-up;*
4. *Participants who are willing to discuss medical history with investigators or doctors and allow access to all medical records relevant to this trial.*
5. *Participants with child-bearing potential who are willing to practice adequate contraception methods from signing the ICF to 12 months after vaccination. This includes:*
   a. *Abstinence from penile-vaginal intercourse,*
   b. *Hormonal contraceptives such as oral contraceptives (the pill), injectables, implants, patches or estrogen vaginal ring (a ring-shaped hormonal contraceptive device that is used inside the vagina),*
   c. *Intrauterine device (IUD/Spiral),*
   d. *Male partner sterilization (vasectomy) prior to the female subject's entry into the study, and this male is the sole partner for that subject,*
   e. *Male condom combined with a vaginal spermicide (a substance that can kill the sperm cells inside the vagina) or female diaphragm, whether with or without a vaginal spermicide.*
6. *Be able to communicate well with the investigator, and to understand and comply with the requirements of this clinical trial.*

Exclusion Criteria

1. *Axillary temperature >37.5°C (99°F).*
2. *Have congenital malformations or developmental disorders, genetic defects, severe malnutrition, etc.*
3. *A history of epilepsy, convulsions or history/family history of mental illness;*
4. *Have meningitis or a history of meningitis illness;*
5. *Positive result of urine pregnancy test (also required for women within one year of menopause), lactating women, or participant /his partner is planning to become pregnant within 1 year.*
6. *Hypersensitivity to a component or excipient of the vaccine used in this clinical trial (mainly: group A, C, Y or W135 meningococcal capsular polysaccharide, diphtheria toxoid or diphtheria antigen, sucrose, mannitol, sodium chloride, dipotassium hydrogen phosphate trihydrate, potassium dihydrogen phosphate).*
7. *In the past 6 months (internal time < 6 months), participants have received immunosuppressive treatment, cytotoxic treatment, glucocorticoid treatment, etc. (excluding local*

treatment, surface treatment of acute non-concurrent dermatitis, spray treatment of allergic rhinitis);

8. *Received or plan to receive blood/plasma products or immunoglobulins throughout the study period or 60 days prior to study vaccination.*
9. *Use of non-prescription drugs such as antipyretic (e.g., acetaminophen) and anti-inflammatory drugs (e.g., ibuprofen, naproxen etc.) within 12 hours before the administration of vaccine.*
10. *Have severe hypertension that is not controlled by medication (at the time of field measurement: systolic blood pressure ≥ 160 mmHg and diastolic blood pressure ≥ 100 mmHg)*
11. *Suffering from a severe chronic disease or a condition that is in a progressive stage and cannot be well controlled, such as thyroid disease*
12. *Participants with known or suspected diseases that are judged by the investigator to affect the vaccination assessment, for example, acute infectious diseases, severe respiratory disease, severe cardiovascular disease, severe allergic skin disease etc.*
13. *History of serious adverse reactions associated with the vaccine and/or history of severe allergic reactions (e.g., systemic allergic reactions) to any component of the study vaccine.*
14. *Immunocompromised individuals with known or suspected immunodeficiency as determined by medical history and/or physical examination (e.g., HIV infection, history of pancreatic, liver, spleen, kidney disease or history of resection).*
15. *Bleeding constitution or condition associated with prolonged bleeding for which intramuscular injection is contraindicated in the opinion of the investigator.*
16. *Administration of live attenuated vaccine within 14 days or other vaccines within 7 days.*
17. *Participation in other studies involving interventional studies within 28 days prior to screening and/or during study participation.*
18. *According to the judgment of the investigator, participants could be excluded due to various medical, psychological, social or other conditions that are contrary to the trial protocol or that affect the subject's ability to sign informed consent.*
19. *Investigator site staff directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members, sponsor staff and their respective family members.*

f. Luaran Uji Klinik/ Endpoint : ***Primary endpoints***

1. *The geometric mean titer (GMT) of serogroup A, C, Y and W135 meningococcal rSBA titer on day 30 post vaccination in all participants.*
2. *The seroconversion rate of serogroup A, C, Y, and W135 meningococcal rSBA titer on day 30 post vaccination.*
   Seroconversion rate for serogroup A, C, Y and W135 was defined as post-vaccination rSBA titers ≥ 1:8 for subjects with pre-vaccination titer < 1:8 or at least 4-fold increase in rSBA titers from pre- to post-vaccination for subjects with pre-vaccination titer ≥ 1:8.
3. *The incidence of adverse reactions (ARs) within 7 days post vaccination in all participants.*

Secondary endpoints

1. *The geometric mean fold increase (GMI) and the proportion of GMT ≥ 1:128 of serogroup A, C, Y and W135 meningococcal rSBA titer on day 30 post vaccination in all participants.*
2. *The incidence of ARs and adverse events (AEs) within 30 days post vaccination in all participants.*
3. *The incidence of ARs within 30 min post vaccination in all participants.*
4. *The incidence of serious adverse events (SAEs) within 365 days post vaccination in all participants.*
5. *The GMT, GMI and the proportion of GMT ≥ 1:128 of serogroup A, C, Y and W135 meningococcal antibodies on day 90, day 180 and day 365 post vaccination in the 480 subjects (Immunopersistence group).*

Ringkasan Hasil Evaluasi

Badan POM telah melakukan evaluasi protokol uji klinik *Group ACYW135 Meningococcal Conjugate Vaccine (CRM197)* yang didukung oleh tim ahli melalui rapat pada tanggal 13 September 2023.

Tersedia data uji klinik fase I pada usia 3 bulan (3 dosis), 6-23 bulan (2 doses), 2-6 tahun (1 dose) dan ≥18 tahun (1 dose) yang menunjukkan vaksin dapat ditoleransi dengan baik dan memberikan respon imun setelah 30 hari *full dose*. Uji klinik dilanjutkan pada fase III menggunakan dosis yang digunakan pada fase I.

Desain uji klinik memadai dan 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 (PPUK) Nomor RG.01.06.1.3.10.23.43 tanggal 26 Oktober 2023.