Philippine COVID-19 Living Clinical Practice Guidelines
Institute of Clinical Epidemiology, National Institutes of Health, UP Manila
In cooperation with the Philippine Society for Microbiology and Infectious Diseases
Funded by the DOH AHEAD Program through the PCHRD

EVIDENCE SUMMARY

Among persons at risk, what is the clinical efficacy, effectiveness and safety of BBIBP-CorV (Sinopharm) in the prevention of SARS-CoV-2 infection?

Evidence Reviewers: Marie Carmela M. Lapitan, MD, Mary Anne Castor, MD, James Paul Gomez, MD

RECOMMENDATIONS

1. We recommend the use of BBIBP-CorV (Sinopharm), given as 200U (WIV04) or 4ug (HBO2) in 0.5 ml in 2 doses, 21 days apart, to prevent symptomatic and asymptomatic COVID-19 infection among healthy adults (18 to 59 years old). *(Moderate certainty of evidence; Strong recommendation)*

2. We suggest the use of BBIBP-CorV to prevent severe COVID-19 infection among healthy adults (18 to 59 years old). *(Low certainty of evidence; Weak recommendation)*

3. We suggest the use of BBIBP-CorV to prevent symptomatic COVID-19 infection in the following:
    a. adults with comorbidities (*Very low certainty of evidence; Weak recommendation)*
    b. older persons (60 years and older) (*Very low certainty of evidence; Weak recommendation)*

4. There is insufficient evidence to recommend for or against the use of BBIBP-CorV to prevent COVID-19 infection among the following:
    a. Children (3-17 years old) (*Very low certainty of evidence)*
    b. Immunocompromised population (*Very low certainty of evidence)*
    c. Pregnant and lactating women (*Very low certainty of evidence)*

5. In areas where the SARS-CoV-2 variants of concern are prevalent, there is insufficient evidence to recommend for or against the use of BBIBP-CorV to prevent COVID. (*Very low certainty of evidence)*

Consensus Issues

The decision of the Panel to defer any recommendation for the use of BBIBP-CorV on children and the immunocompromised was based on the limited evidence of efficacy. As no correlate of protection has been established for COVID-19 vaccines, the Panel did not feel that immunogenic response was sufficient to make a recommendation, especially from studies with a small number of participants. The same issue was considered in withholding a recommendation with the use of BBIBP-CorV against the SARS-COV-2 variants of concern.

Key Findings

The evidence base for the clinical efficacy, effectiveness, and safety of BBIBP-CorV (Sinopharm), as of October 29, 2021 included one network meta-analysis, four randomized controlled trials, 14 observational studies and two regulatory authority reports. Trial results showed that BBIBP-CorV, particularly the HB02 formulation, provided sufficient protection against symptomatic and asymptomatic COVID-19 infection, within a follow up period of 77days. Limited information was available regarding effectiveness against severe infection and on protection for the older population. Immunologic studies show that the vaccine is immunogenic even among children. Limited information from observational studies on the

effectiveness of the vaccine for the immunocompromised suggested some protection and immunogenicity. Available safety data shows acceptable safety profile with no adverse event of interest reported.

Introduction

Despite the global roll out of COVID-19 vaccines beginning last quarter of 2020, the development of novel vaccines against SARS-CoV-2 continue. Among the many vaccine platforms, inactivated vaccines are the most extensively studied. It is considered safe and are widely used for the prevention other respiratory infections. It is also easily stored and shipped, making it suitable for wide use in low-resourced countries such as the Philippines.

BBIBP-CorV, an inactivated viral vaccine based on the HBO2 strain, was developed through a collaboration between the Chinese Center for Disease Control and Prevention and the Beijing Institute of Biological Products (BIBP)/China National Biotec Group Company Limited (CNBG). Two formulations of the vaccine has since been developed using two different strains, the HB02 and the WIV04. The latter strain was developed by the Wuhan Insitute of Biological Products, also in collaboration with CNBG. Both are offered as a two-dose regimen, 21 to 28 days apart.

BBIBP-CorV (Sinopharm) was first granted Emergency Use Authorization by the Philippine Food and Drug Administration (PFDA) on August 19, 2021.[1] As of October 24, 2021, 750,978 doses have been administered in the country.[2]

This review describes the current available evidence supporting the efficacy, effectiveness and safety of BBIBP-CorV in the prevention of COVID-19.

Review Methods

General Search Results

As of October 29, 2021, 19 studies and 2 regulatory reports were identified as providing information on the performance of BBIBP-CorV as a vaccine against SARS-CoV-2. One network meta-analysis presented the neutralizing antibody response of BBIBP-CorV in relation to the other vaccines.[3] Four studies were randomized controlled trials, one providing both clinical and immunologic efficacy and safety,[4] and the rest providing immunologic and safety outcomes.[5-7] Two studies provided data on the performance of BBIBP-CorV against variants of concern.[8-9] Five observational studies were on the immunocompromised population. One study reported on the immunogenic outcomes of a booster dose.[10]

The risk of bias assessment of all included studies are in Table 2.

Results

Clinical Efficacy

The pivotal Phase 3 trial establishing the efficacy and safety of BBIBP-CorV involved over 41,000 health adults, with over 26,000 receiving the vaccine (WIV04=13,459; HBO2=13,465). Results after a median follow up of 77 days (112 days as per WHO-SAGE report) showed sufficient protection against COVID-19 infection. Vaccine effectiveness (VE) against symptomatic COVID-19 infection was reported as 72.8 (95% CI 58.1-82.4) for WIV04 and 78.1 (95% CI 64.8-86.3) for HB02. On the other hand, VE against any infection (i.e. including asymptomatic infection) were 64.0 (95 %CI 48.8-74.7) for WIV04 and 73.5 (95% CI 60.6-82.2) for HB02. Severe infection was noted only in 2 cases, both in the control group precluding any estimation of VE for this outcome.[4]
Table 3 details the characteristics of the pivotal trial for BBIBP-CorV. Detailed outcomes are in Table 9 and 10.

Immunogenicity

A network meta-analysis on neutralizing antibody responses across the different COVID-19 vaccines included 11 studies, of which one used BBiBP-CorV. BBIBP-CorV was considered to produce very large effect on the level of neutralizing antibodies (SMD >1.3), similar with the ChAdOx1 (AstraZeneca), BNT162b2 (Pfizer), and Gam-COVID-Vac (Sputnik V).[3]

The reference trial in the above NMA was the Phase 1/2 trial of BBIBP-CorV (HB02) on healthy adults that investigated on the immunogenicity of varying doses and dosing intervals. In this study, neutralizing antibody titers were significantly increased in those who received the vaccine compared with the control. Titers were noted to higher in the young (18 to 59 years old) compared to the older population. Titers were higher after the two-dose 4ug regimen, compared with the single dose 8ug.[6]

Another Phase 1/2 RCT using BBIBP-CorV involved children aged 3 to 17 years, showing significant increase in neutralizing antibody titers after 2 doses of the vaccine with no further increase after the third dose, and with the 4ug and 8ug doses having higher titers than the 2ug dose. All treatment groups reached 100% seropositivity.[7]

One randomized controlled trial involving healthcare workers compared the immunogenic responses of two doses of BBIBP-CorV at 14-, 21-, and 28-day intervals. The three groups showed 100% seroconversion. Those in the 21- and 28-day interval elicited significantly higher neutralizing antibody levels compared to those in the 14-day interval group.[5]

In a longitudinal study among healthcare workers, 100% seroconversion for anti-spike specific antibodies was observed after the second dose of BBIBP-CorV. Three months later, titers significantly dropped but still significantly higher than pre-vaccination. This study also showed that previously infected individuals generated significantly higher titers after BBIBP-CorV vaccination at all timepoints compared to the infection-naïve.[11]

A prospective study involving mostly elderly vaccine recipients suggested decreased immune response from BBIBP-CorV in the older population. (see below)[12]

Immunogenicity of BBIBP-CorV among immunocompromised population is discussed in the section below.

Real World Evidence: Effectiveness

General Population

Two studies on the real-world clinical effectiveness were identified, limited to reporting breakthrough infections after BBIBP-CorV vaccination. One was a prospective cohort on 82 healthcare workers which reported four cases of infection after the first dose, two immediately after the second dose, and two getting the infection more than 14 days after second dose. It was unclear how long the follow up was in this study.[11]

A case series involving an extended family of 54 members showed only partial protection provided by BBIBP vaccination. Nearly all vaccinated members developed breakthrough infection. Hospitalization was necessary in 43% (10/23) of those who received only one dose whereas it was needed in only 5% (1/20) in those who received two doses. The only death in the study was from among the unvaccinated members.[13]

Clinical Efficacy and Effectiveness On Special Populations of Interest (Older persons, Children, Immunocompromised, Pregnant Women)

Older population

Older persons (>=60 years of age) were recruited late in the Phase 3 trial and thus composed only a small proportion of the study population included (WIV04=213, HB02=201) in the interim report with shorter follow-up duration. No events were recorded in both the vaccine and placebo groups during the observation period of the trial report, precluding any estimation of vaccine efficacy in this group.[4,14] In the Phase 1 trial, neutralizing antibody titers were noted to be significantly less in the older population compared to the young.[6]

The lower immunogenic response to BBIBP-CorV among the older persons was also shown in a prospective cohort study 450 BBIBP-CorV vaccinees, mostly elderly individuals who requested for antibody measurements after a median follow up of 23 days after the second dose. This study demonstrated that increasing age correlated with a lack of antibody production with the estimated probability of the lack of antibody response at 25% for those aged 60 years and 50% for those aged 80 years old. When compared to a randomly selected sample from 50 BNT162b2 vaccinees, antibody titers with BBIBP-CorV were significantly lower in this study.[12]

Children

Since children were excluded in the regulatory trial, no clinical efficacy data was found for children. Only immunogenicity data was available.

A Phase 1/2 placebo-controlled RCT involving children from 3 to 17 years compared immunogenic responses to three different doses (2, 4, and 8ug) given as three doses (day 0, 28, and 56). All groups reached 100% seroconversion. However, significantly higher titers were seen in those who received 4ug and 8ug dose compared to 2ug after the first and second doses. The titers were similar after the third dose.[7]

Pregnant women

Pregnant women were excluded in the clinical trial of BBIBP-CorV. However, the WHO SAGE report noted that in the Phase 3 trials submitted for the review, five pregnancies were reported in the vaccine group (HB02). At the time of the SAGE review, pregnancy and birth outcomes were still being monitored.[14]

Immunocompromised

Five studies involving the immunocompromised were found. Three involved patients with multiple sclerosis,[15-17] one on patients on dialysis[18] and one on cancer patients.[19]

Two studies among multiple sclerosis patients focused on safety outcomes of BBIBP-CorV vaccination. One study reported that 16.2% had at least one neurologic side effect during the at-risk period (most common were motor symptoms and vertigo). Six (1.2%) vaccinees experienced relapse during the at risk period.[15] Another study followed 583 patients with multiple sclerosis after 1 dose of BBIBP. No serious adverse event was reported. At least one transient symptom was experienced by 60% of vaccines including constitutional symptoms (51%) and headache (9%). Five (0.9%) reported relapse after vaccination.[16]

One small series of multiple sclerosis patients on disease modifying therapies showed seroconversion rates of 42-100%.[17]

One study on dialysis patients receiving 2 doses of BBIBP-CorV (HB02 strain) reported an overall case fatality rate in vaccinated individuals as 4.3% (8/187), compared to 8.7% (28/324) in the unvaccinated. Serologic studies performed in a subgroup of 270 patients who were

seronegative at baseline showed that 41% had suboptimal levels 14 to 21 days after the second dose.[18]

Cancer patients with solid and hematological tumors (n=364) were given two doses of BBIBP-CorV. Overall seropositivity rates were high (80.7% for neutralizing antibodies, 77% for anti-IgG). Seroconversion was found to be higher in patients with breast cancer (93.3%) and upper GI cancers (94.7%). Lowest rates were found in patients with hematologic malignancies (61.9%). The rate of seroconversion was higher in patients less than 60 years old. Local side effect rate was 15% and these were mostly mild. Severe local side effect was experienced by 2.2%. The most common systemic side effect was fever (31.6%). One patient (2.7%) experienced breakthrough infection after the first dose and three (8.3%) after the second dose.[19]

Safety

Regulatory Clinical Trial Evidence

Four randomized trials provided safety data, one of which involved children. All were consistent in demonstrating adverse event rates after BBIBP-CorV as comparable with the control.[4-7] Overall adverse event rates (including adverse reactions) ranged from 3.2% to 45%. Unsolicited adverse event rates within 28 days ranged from 3.7% to 29%. The most common local adverse reaction was pain at the injection site. The Phase 2 trial in children found a dose dependent increase in local pain at injection site compared with placebo.[7] Fever and headache were the most common systemic adverse reaction. All adverse reactions were mild to moderate. No serious adverse events were reported in 3 trials and was only 0.4-0.5% in the Phase 3 trial, which were similar to the control group. Two serious adverse events were assessed to be possibly related to the HB02 vaccine. One was a demyelinating disease developing in a 50 year old man after the first dose and one was a case of severe emesis in a 35-year old woman after the second dose.[4] One case of allergic purpura in a child assessed as severe and vaccine related was noted after the second BBIBP-CorV dose.[7]

Detailed safety outcomes from the Phase 3 trial are in Table 9.

Real World Evidence of Safety

Three studies were found reporting on real world evidence on safety of BBIBP-CorV. The rates found in these studies were consistent with those in the clinical trials. Two were surveys done using online platforms. Both showed adverse reaction rates similar to those found in the clinical trials. The first compared adults vaccinated with BBIBP-CorV (n=513) and BNT162b2 (n=491).[20] The second study analyzed 1080 survey responses from those who received at least one dose of BBIBP-CorV. Most of the respondents were female. Injection site pain was the most common adverse event. Twenty four percent of the respondents did not have any adverse events after vaccination.[21]

One prospective study among 406 healthcare workers was specifically performed to determine the incidence of thrombotic events and to determine any change in the presence of autoantibodies pre- and post-vaccination. After an eight-week follow up, no thrombotic event occurred. No significant difference was noted in the presence of all 10 autoantibodies between pre- and post- vaccination samples. Seven cases presented with anti-PF4 heparin antibodies but none of them exhibited any sign of thrombotic disorder.[10]

In the October 24, 2021 report of the Philippine Food and Drug Administration, 86 adverse events were associated with BBIBP-CorV (Sinopharm), after 750,978 doses administered locally. Five of these were classified as serious, with no further description of the cases given.

The top reported events were pyrexia (25.6%), cough (15.1%), dizziness (13.95%), and headache (13.95%).[2]

Reports on Adverse Events of Interest

The WHO SAGE report cited two cases of Bell's palsy in the trial, one in the placebo group and one in the BBIBP-CorV group. One thrombotic event was reported among the 29,240 trial participants in the vaccine group. This was in a 50 year old man who had prior history of blood clots before vaccination and suffered abdominal pains 7 days after the first dose of BIBP, confirmed to be due to a thrombus.[14]

Effectiveness Against Variants

Two studies investigated the effectiveness of BBIBP-CorV against the variants of concern based on immunogenic response. The first study used 12 random serum samples from trial patients extracted 28 days after the second dose of BBIBP-CorV. It found a 1.6-fold reduction in GMTs against the Beta variant compared to the Wuhan strain.[8] The second study involving 282 infection-naïve vaccinees showed significantly lower titers to Alpha (1.3-fold reduction), Beta (10-fold) and Delta (1.38-fold) compared to WT at 2 weeks after the second dose of BBIBP-CorV.[9]

Tables 9 and 10 present the summary of findings and certainty of the evidence for BBIBP-CorV.

Duration of Protection

One prospective study on 82 healthcare workers demonstrated that anti-spike specific antibody titers significantly dropped three months after the second dose, but still to a level higher than after the first dose. The decline was greater in those without prior infection.[11]

Booster Vaccination

One study investigated the effect of a booster dose of BBIBP-CorV six months after the primary vaccination in 50 volunteer healthcare workers. It showed increased neutralizing antibody titers peaking at two weeks post-boost with a 10.6 fold rise. All antibodies (anti-spike, RBD, N) were detectable post-boost. B cells for spike and RBD were likewise increased post-boost. T-cell response was enhanced by the boost by 2.3-fold. In those who remained seronegative after the primary vaccination, seroconversion for neutralizing antibodies, B-cell and T-cell responses were noted post boost but to a lesser extent compared to those who responded to the primary vaccination.[22]

Authorizations

The Philippine FDA has issued three EUAs for BBIBP-CorV (Sinopharm) from 3 manufacturers on August 19, 2021 (WIV04–WIBP), on September 10, 2021 (HB02 – BIBP), and on October 14, 2021 (Hayat-Vax, strain unspecified).[23]

The WHO has included BBIBP-CorV (Sinopharm) in its emergency use listing based on the SAGE recommendations (only for HB02) for its administration to 18 years and above (2 doses at interval of 3 weeks but with flexibility to extend to 4-week intervals) on May 7, 2021. In its updated guidance on October 28, 2021, the WHO-SAGE indicated that additional dose of the vaccine may be needed as part of an extended primary series for populations where the

immune response following the standard primary series is deemed likely to be insufficient, such as the older persons and immunocompromised individuals.[24]

Research Gaps

The following are identified research gaps regarding BBIBP-CorV vaccination for COVID-19 infection prevention: The efficacy/effectiveness of BBIBP-CorV in special populations such as the older and very old patients, children, immunocompromised (eg. HIV) populations; the duration of protection / long term efficacy or effectiveness; its long-term safety; its clinical efficacy and effectiveness against infection with variants of concern; studies on heterologous primary vaccination; and its use in booster vaccinations.

Ongoing Trials

The search performed on October 31, 2021 of the Clinicaltrials.gov registry showed eight trials on BBIBP-CorV (Sinopharm). Table 11 details these trials.

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Appendix 1: Evidence to Decision

Table 1. Summary of Judgements Prior to Panel Discussion (N=7)

FACTORS	JUDGEMENT						RESEARCH EVIDENCE/ADDITIONAL CONSIDERATIONS
Problem	No	Yes (7)					
Benefits	Large	Moderate (6)	Small	Uncertain (1)			• In a Phase 3 trial involving 41,000 healthy adults: Vaccine effectiveness (VE) against symptomatic COVID-19 infection was reported as 72.8 (95% CI 58.1-82.4) for WIV04 and 78.1 (95% CI 64.8-86.3) for HB02.
Harm	Large	Small (5)	Uncertain (2)				• Four randomized trials were consistent in demonstrating adverse event rates after BBIBP-CorV as comparable with the control. • Overall adverse event rates (including adverse reactions) ranged from 3.2% to 45%. The most common local adverse reaction was pain at the injection site. • Isolated case reports from WHO SAGE include: 2 cases of Bell's palsy and 1 thrombotic event.
Certainty of evidence	High	Moderate (4)	Low (3)	Very Low			• Very low to high
Balance of effects	Favors vaccine (5)	Does not favor vaccine	Uncertain (2)				
Values	Important uncertainty or variability	Possibly important uncertainty or variability (3)	Possibly no important uncertainty or variability (3)	No important uncertainty or variability (1)			

Resources required	Uncertain	Large cost	Moderate cost (6)	Negligible cost or savings	Moderate savings (1)	Large savings	• Sale price of Sinopharm varies from $19-$36 (PHP 950-PHP 1820). • The required storage temperature for Sinopharm is 2-8 degrees Celsius, not allowed to be frozen. It must be protected from light.
Certainty of evidence of resources required	No included studies (7)	Very low	Low	Moderate	High		
Cost effectiveness	No included studies (7)	Favors the comparison	Does not favor either the intervention or the comparison	Favors the intervention			
Equity	Uncertain (2)	Reduced	Probably no impact	Increased (5)			• PHL FDA EUA indication is for clinically healthy people (aged 18 years old and above) susceptible to the virus. • Addresses wide disparity in vaccine coverage: 85.1% fully-vaccinated senior citizens in NCR; only 28.3% in BARMM
Acceptability	Uncertain (1)	No	Yes (6)				• BBIBP-CorV (Sinopharm) was granted Emergency Use Authorization by the Philippine Food and Drug Administration (PFDA) on August 19, 2021.
Feasibility	Uncertain (1)	No	Yes (6)				

Appendix 2. Risk of Bias Assessment of Included Studies

Study ID	Design	Randomization	Allocation Concealment	Blinding Particip	Blinding Carer/ Assessor	Followup	Selective Reporting	Others	Age	Comorbidities	Exposure	Confounding	OVERALL
Abu-Halaweh (Jordan)	Prospective cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Al Kaabi (UAE, Egypt)	RCT Ph3	LOW	LOW	LOW	LOW	HiGH	LOW	NA	NA	NA	NA	NA	SOME CONCERNS
Ariamanesh (Iran)	Single cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Badano (Argentina)	Single cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Drulovic (Serbia)	Single cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	HiGH	HiGH	HiGH	HiGH	HiGH	VERY SERIOUS
Etemadifar (Iran)	Prospective cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	HiGH	HiGH	HiGH	HiGH	HiGH	SERIOUS
Feng (China)	RCT Ph4	LOW	UNCLEAR	UNCLEAR	UNCLEAR	HiGH	LOW	NA	NA	NA	NA	NA	SERIOUS
Ferecii (Hungary)	prospective cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Holt (UAE)	Prospective cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	NA	NA	NA	NA	NA	SERIOUS
Huang (China)	Single cohort	HiGH	HiGH	HiGH	UNCLEAR	UNCLEAR	UNCLEAR	HiGH	HiGH	HiGH	HiGH	HiGH	SERIOUS
Jahromi (Bahrain)	Single cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	HiGH	HiGH	HiGH	HiGH	HiGH	VERY SERIOUS
Jeewandara (Sri Lanka)	Single cohort	HiGH	HiGH	HiGH	UNCLEAR	LOW	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Liu (China)	Single cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Liu Y (China)	Single cohort	HiGH	HiGH	HiGH	HiGH	LOW	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Saeed (UAE)	Single cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Sahraian (Iran)	Single cohort	HiGH	HiGH	HiGH	HiGH	HiGH	UNCLEAR	NA	HiGH	HiGH	HiGH	HiGH	SERIOUS
Xia1 (China)	RCT Ph 1/2 (Adult)	LOW	LOW	LOW	LOW	LOW	UNCLEAR	NA	NA	NA	NA	NA	NOT SERIOUS
Xia2 (China)	RCT Ph 1/2 (Children)	LOW	LOW	LOW	LOW	LOW	UNCLEAR	NA	NA	NA	NA	NA	NOT SERIOUS

Appendix 3. Characteristics of the Randomized Controlled Trial (Ph3) on the Efficacy and Safety of BBIBP-CorV

Trial Identifier	**ChiCTR2100041705, ChiCTR2100041706**
Vaccine	**BBIBP-CorV (Sinopharm)**
Data Sources	**AlKaabi (main paper, protocol and supplement), WHO SAGE Background Report**
POPULATION	
Total Randomized	40,411
Inclusions	18 years and above, judged as healthy
● Age	18 years and above, but older (>60 years) recruited late in the study
● Gender	Both: 84.4% men
● Race/Ethnicity	Multicountry: 23.3% UAE
● Immunocompromised	Excluded
● Pregnant and breastfeeding	Excluded
● With concomitant comorbidities	Excluded
● With previous COVID infection	Excluded
● With known previous exposure to COVID	Not mentioned
● Seropositive at baseline	6.4%
Exclusions	Acute cases of SARS-CoV-2 infection, with medical history of SARS or MERS, fever, positive urinary pregnancy, with previous severe allergic reactions or known allergy to inactivated SARS-CoV-2 vaccine, with medical history or family history of convulsion, epilepsy, encephalopathy or mental illness, congenital malformation or developmental disorder, genetic defects, severe malnutrition, known or suspected acute respiratory disease, severe cardiovascular disease, severe liver disease, severe kidney disease, uncontrollable hypertension, diabetic complications, malignant tumors, acute diseases, diagnosed with congenital or acquired immune deficiency, HIV infection, lymphoma, or other autoimmune diseases, history of coagulation dysfunction, receiving anti-TB therapy, receiving immune enhancement or inhibitory therapy within 3 months, vaccinated live attenuated vaccine within 1 month before, received blood products within 3 months, received other investigational drugs
INTERVENTION (VACCINE)	
Type	Inactivated virus
Active substance	Inactivated SARS-CoV-2 (WIV04 or HB02 strain) in aluminum hydroxide adjuvant
Storage and Cold chain considerations	
● Shipping and transport	2-8’C

● Storage and shelf life prior to dilution/ opening	2-8'C
Final product	
Form and use	WIBP: 200U/dose BIBP: 4ug/dose
Excipients	aluminum hydroxide adjuvant
Trial-specific considerations	
Dosing and administration	WIV04 (WIBP), 200WU/dose in 0.5ml, 2 doses 21d interval (+7) HB02 (BIBP), 4ug vp/dose in 0.5ml, 2 doses 21d interval (+7)
Number randomized	WIV04 (WIBP) = 13470 (13066 received D2) HB02 (BIBP) = 13470 (13086 received D2)
COMPARATOR	
Type, dosing and administration	Aluminum adjuvant, 0.5ml, 2 doses 21d interval (+7)
Number randomized	13,471 (13,071 received D2)
OUTCOMES	
Primary efficacy endpoints	Vaccine efficacy against COVID-19 (symptomatic infection) 14 days following 2 doses, confirmed cases confirmed by EAC blinded review
Primary safety endpoints	- incidence of any adverse reactions/events within 30 mins after each dose - incidence of solicited adverse reactions within 7 days - unsolicited adverse reaction with d8-21 after first dose and d8-28 after 2nd dose - incidence of serious adverse events from D1 to 12 months
Secondary endpoints Exploratory endpoints Immunogenicity	- Vaccine efficacy against severe cases and deaths - Anti-SARS-CoV-2 neutralizing antibody protective level against COVID-19 - Occurrence of ADE/VED after immunization - 4-fold increase rate, GMT and GMI of anti-SORS-COV-2 neutralizing antibody in after full course of immunization: 14d, 28d, 3 mos, 6 mos, 9 mos, 12 mos
Post Hoc	- asymptomatic infection - infection after first dose, before second dose
Subgroups considered in the analysis	
● Age	>60 years old (only 213 in WIV04 and 201 in HBO2, and 198 in alum), but cases during the study so no efficacy was calculated
● Sex	No
● Ethnic groups	No
● Baseline seropositivity status / evidence of previous infection	Noted outcomes but too small to do subgroup analysis, only 1 case in the alum group
● Medical comorbidities	No
● Immunocompromised / HIV disease	excluded
● Risk for acquiring COVID infection	no

• Risk for progression to severe COVID	no
• Dosing regimen	21 day interval (+7 days)
Follow up	
• Planned	1.5 years
• At data cutoff of interim report (first interim analysis)	Median duration 77 days (1-121) * WHO report : 122 days
Date of Data Cut-off date for latest available trial data	December 20, 2020
METHODS / OTHER TRIAL PARAMETERS	
Blinding	No mention
Study Sites	China
Study Sponsor	China National Biotec Group Company Ltd, Wuhan Institute of Biological Products, Beijing Institute of Biological Products
Type of report available as of this rapid review	Full publication with supplement
Others	Balanced withdrawal/ late exclusions across groups including reasons for exclusion

Appendix 3. Characteristics and Results of Clinical Trials on BBIBP-CorV

Study ID	Design	Population	Intervention / Comparison	Outcome (Followup/Assessment) Result
Al Kaabi	RCT (Interim analysis)	>18yo without any history of COVID-19 WIV04 = 13,459 HBO2 = 13, 465 Alum = 13, 458	2 doses of either WIV04 and HB02 (21 days apart) Control: Aluminum hydroxide	VE of WIV04 / HB02 Symptomatic: (median ffup: 77days) 72.8 (58.1-82.4) / 78.1 (64.8-86.3) Severe: (median ffup: 77days) 100% / 100% (2 cases in placebo) Asymptomatic: (median ffup: 77days) 64.0 (48.8-74.7) / 73.5 (60.6-82.2) GMT d14 after 2nd dose WIV04: 94.5 (89.7 – 99.5) HB02: 156 (149.6 – 162.7) Placebo: 2.7 (2.6 – 2.8) Seroconversion d14 after 2nd dose WIV04: 99.3% HB02: 100% WIV04 / HB02 / placebo Total AR rate: 44.2 / 41.7 / 46.5% Pain at injection site: 24.3 / 19.4 / 27.9% Headache: 12.9 / 13.1 / 12.6 No increase in solicited AE during 8-28 days after injection Unsolicited AE increased: 11.1-16.1 / 10.7 - 15.5 / 10.6-15.4 Total AE: 48.3 / 46.1 / 50.5 SAE: 0.5% / 0.4% / 0.6% *Related SAE, both in placebo: demyelinating myelitis after D1 and severe emesis after D2

Xia 1	RCT	Healthy adults Ph1: 18 to 80 y/o Ph2: 18 to 59 y/o	BBIBO-CorV (HBO2) Ph1: 2 dose (28d) 2, 4, 8ug Ph2: 8 ug (1d) 4 ug (14, 21, 28d) control: placebo (alum with saline)	Ph1: at least 1 AR: 29%, all mild to moderate no serious AE with 28 days most common systemic AR: fever, no difference across groups NaB, significantly higher than placebo but titers higher in the young (18-59yo) compared to the older Ph2: at least 1 AR: 23% higher rate with 8ug, decreasing rate in increasing dosing interval most common systemic AR: fever, no difference across groups NAB higher with 2 doses, highest with 4ug
Xia 2	RCT	3 to 17 y/o. Ph 1 = 216 Ph 2 = 810 (Vac = 540, pla = 180)	BBIBP-CorV doses: 2, 4, 8 ug 3 dose schedules (0, 28, 56) control: placebo (alum with saline)	dose dependent increase in overall injection site ARs in vaccine groups compared with control most common systemic reaction was fever (12.7%) and cough (8.7%); not different from placebo only 1 vaccine related AE = grade 3 allergic purpura after D2 in 6-12 yo cohort significantly higher titers with 4 and 8ug compared to 2ug after D1 and D2 but all the same at D3

Feng et al.	RCT	18-59yo in the occupational high-risk population N = 809 14 day: 270 (256 ffup) 21d: 270 (247 ffup) 28d: 269 (241 ffup)	BBIBP 4ug at 14, 21, or 28-day intervals (Strain not specified)	Seroconversion of neutralizing antibodies (28days pD2) PP 14d: 100% 21d: 100% 28d: 100% ITT 14d: 94.8% 21d: 91.5% 28d: 89.6% GMT (28 days pD2) PP 14d: 98.4 21d: 134.4 28d: 145.5 ITT 14d: 93.5 21d: 122 28d: 129.8 *The same trend of having lower seroconversion rate in the 14day group compared to the other groups was seen even if different cutoff values were used. Overall AE rate 14d: 4.1% 21d: 4.8% 28d: 3.7% Solicited AR: 3.2% Unsolicited AE: 0.99% No significant difference across 3 dosing groups No reported serious AE

Appendix 5. Characteristics of Studies on the Real-World Evidence of BBIBP-CorV (EFFECTIVENESS, General Population and immunocompromised)

Study ID	Design	Population	Intervention	Comparison	Follow up	Outcomes Reported
Jahromi et al.	Case series	54 members of an extended family	BBIBP 26 partially vacc 20 fully vacc	Unvaccinated (n=8)		(Total) Infection / Hospital / Death Unvaccinated: 8 / 3/ 1 Partial: 23 /10 /0 Fully: 20 / 1 /0
Holt	Comparative cohort	Patients on dialysis with negative baseline titers (n=187)	2 doses of BBIBP (HBO2) 21-day interval (+7 days)	Unvaccinated (n=234)	14-21 days after 2nd dose	Case fatality rate Among unvaccinated: 8.7% (28/324) Among vaccinated: 4.3% (8/187)

Appendix 6. Characteristics of Studies on the Real World Evidence of BBIBP-CorV (SAFETY, General Population and Immunocompromised)

Study ID	Design	Population	Intervention	Comparison	Follow up	Outcomes Reported
Saeed	Cross-sectional survey (Self-administered via social media sites)	1080 responses, general population	One or 2 doses of BBIBP (Strain not specified)	none		24.4% did not have any side effects After 1st dose Site pain (42.2%), fatigue (12.2%), headache (9.6%) After 2nd dose Site pain (32.6%), fatigue (16.3%), lethargy (13.7%) SE after both doses were more prevalent in <49yo group. More females suffered from SE than males.
Etemadifar	Prospective cohort	Subjects with multiple sclerosis (Vaccinated: 517) (Unvacc: 174)	2 doses of BBIBP (Strain not specified)	Unvaccinated	At-risk period: Vaccinated cohort - 2 weeks after 1st dose and 2 weeks after 2nd dose Unvaccinated cohort – 1-year period before the study	16.2% (n = 84) of vaccinated had at least one neurologic side effect during the at-risk period (most common were motor symptoms and vertigo) Six vaccinees experienced MS relapse during the at-risk period. No significant difference between relapse rates of vaccinated and unvaccinated subjects in the year prior. No SAE reported.

Sahraian et al.	Cross-sectional study using a questionnaire via social networks	583 subjects with multiple sclerosis	1 dose of BBIBP (Strain not specified)			No serious AE At least one transient complaint by 60% of vaccinees Most common are constitutional symptoms (51%), headache (9%) Only 5 (0.9%) reported MS relapse after vaccination
Ariamanesh et al.	Single cohort using questionnaire survey	Adult patients with cancer (N = 364)	2 doses of BBIBP (Strain not specified)		2 months after 2nd dose	Local SE Mild: 5.4% Severe: 2.2% Most common systemic SE: fever (31.6%)

Appendix 7. Characteristics and Results of Studies on the Immunogenicity of BBIBP-CorV (Observational studies)

Study ID	Population (n)	Vaccine Regimen	Extraction time	Result
Liu	Healthcare workers N = 50	2 doses of BBIBP with a 28-day interval and a third booster shot six months after prime vaccination (Strain not specified)	d180 before boost d187, d194, d208 after boost	Six months after primary vaccination, 36/50 tested negative for NAB Serologic response induced within 1 week of booster dose. Peak concentration of NAbs reached at 2 weeks (10.6-fold rise) All antibodies (anti spike, RBD, N) were detectable post boost. Increased B cells post boost (for spike and RBD B cells) CD8 and CD4 T cell response enhanced by booster 2.7- and 5.9-fold respectively. In those who remained seronegative after the primary vaccination, seroconversion for NAb, B-cell and T-cell response was noted post boost but to a lesser extent compared to those who responded to the primary vaccination. NAb levels peaked at 2 weeks after the boost.
Badano	Healthcare workers with or without exposure to SARS-COV-2 N = 82	2 doses of BBIBP (Strain not specified)	21 to 30 days after 1st dose and 2nd dose 3 months after 2nd dose	100% seroconversion for anti-S IgG after D2 (40% after D1) Significant increase in titers after D2 Significant drop in titers after 3 months 4 infections after D1, 2 immediately after D2, 2 more than 14 days after D2
Jeewandara	282 participants (seronegative at baseline)		2 weeks after 2nd dose	95% seroconversion overall Lower seroconversion rates with individuals >60yo vs 20-39 yo (93.3% vs 98.9%); higher in males, no diff in those with comorbidities

Holt	Patients on dialysis with negative baseline titers N = 270	2 doses of BBIBP (HBO2) 21-day interval (+7 days)	14-21 days after 2nd dose	Positive anti-spike antibodies: 56.5% (41% had suboptimal antibody levels) Overall GM anti-spike: 13.3 (11-15.8) Overall GM NAb: 13 (10.9-15.6)
Ariamanesh	Adult patients with cancer (N = 364)	2 doses of BBIBP (Strain not specified)	2 months after 2nd dose	NAb seropositive: 80.7% antiS IgG seropositive: 77.1% 1 patient tested (+) after D1, 3 tested (+) after D2 Rate of seroconversion was higher in patients <60yo. Rate of seroconversion higher in patients with breast cancer (93.3%) and upper GI cancers (94.7%). Lowest rates were found in patients with hematologic malignancies (61.9%). Antibody response higher in those receiving radiotherapy alone or endocrine therapy (97%) compared to those in chemotherapy (83.5%).

Appendix 8. Characteristics and Results of Studies on the Immunogenicity of BBV152 against Variants of Concern

Study ID	Population (n)	Test used (Timing of Extraction)	Variants Tested	Reference strain	Result
Huang	12 trial participants	Geometric mean titre (GMT)	Beta (501Y.V2)	WT or D614G strain	All samples showed preserved neutralization against the Beta variant Compared with titers against WT or D614G strain, GMT from BBIBP decreased from 110.9 to 71.5, or a 1.6-fold reduction Reduction is significantly less than those reported from convalescent plasma or antisera from mRNA vaccine recipients.
Jeewandara	282 participants (seronegative at baseline)	Anti-RBD antibodies	Alpha Beta Delta IFN-gamma at 2 weeks after second dose (N=66)	anti-RBD antibodies to WT, Alpha, Beta and Delta	95% seroconversion overall Lower seroconversion rates with individuals >60yo vs 20-39 y/o (93.3% vs 98.9%); higher in males, no diff in those with comorbidities At 6 weeks (2 weeks post D2), there were significantly less titers to Alpha (1.3-fold red), Beta (10-fold) and Delta (1.38-fold) compared to WT. Noted increased T and B cell response at 2wks post D2 but less than those observed with some other vaccines.

Appendix 9. Summary of Findings Table on the Efficacy of BBIBP-CorV

Efficacy Outcome (at >14 days after dose2)		Quality Assessment					Summary of Findings			Certainty
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Overall Assessment	Vaccine n/N (%)	Control n/N (%)	Vaccine Efficacy (CI)	
1: Symptomatic COVID-19 infection, seronegative at baseline	RCT	Some concerns (Short ffup)	Not assessed	Not serious	Not serious	Some concerns	26/12743 [a] 21/12726 [b]	95/ 12737	72.8[a] (58.1-82.4 78.1[b] (64.8-86.3)	+++ Moderate
2 : Severe COVID-19 infection, seronegative at baseline	1 RCT	Serious Short ffup	Not assessed	Not serious	Serious (Low case numbers	Serious	0/12743 [a] 0/12726 [b]	2/12737	100% (NE)	++ Low
3. Asymptomatic COVID-19 infection, seronegative at baseline	1 RCT	Serious (Short ffup)	Not assessed	Not serious	Not serious	Serious	16/12727 [a] 10/12713 [b]	21/12722		+++ Moderate
4. Any COVID-19 infection, seronegative at base line	1 RCT	Serious (Short ffup)	Not assessed	Not serious	Not serious	Serious	42/12727 [a] 31/12713 [b]	116/12722	64.0 [a] (48.8-74.7) 73.5 [b] (60.6-82.2)	+++ Moderate
5. Symptomatic COVID-19 infection after first dose, before the second dose	1 RCT	Serious (Short ffup)	Not assessed	Not serious	Not serious	Serious	43/12727 [a] 27/12713 [b]	43/12722	50.3% [a] (33.5-62.7) 65.5% [b] (52.0-75.1%)	+++ Moderate
6. Symptomatic COVID-19 infection, older adults (>=60yo), seronegative at baseline	1 RCT OBS	Serious Short ffup	Not assessed	Serious (immuno)	Serious (Low case numbers	Very Serious	No reported events in the Ph3 trial; Immunologic studies showed significantly lower titers in the older population; 1 observational immunologic study showed 25-50% probability of seronegativity in the older population			++ Very Low
7. Symptomatic COVID-19 infection, with pre-existing medical condition	2 OBS	Serious Short ffup	Not assessed	Serious (population data)	Not serious	Serious	Estimates of VE in studies from general population, assuming inclusion of persons with comorbidities, show similar rates with clinical trials on healthy persons			++ Low
Efficacy		**Quality Assessment**					**Summary of Findings**			**Certainty**

Outcome (at >14 days after dose2)		Risk of Bias	Inconsistency	Indirectness	Imprecision	Overall Assessment	Vaccine n/N (%)	Control n/N (%)	Vaccine Efficacy (CI)	
8. Symptomatic COVID-91 infection, children (<18yo)	1 RCT	Serious Short ffup	Not assessed	Serious (Immuno)	Not assessed	Very Serious	Significant immunogenic response observed, with significant increases in humoral and cellular responses			++ Low
9. Any COVID-19 infection, B.1.1.7/Alpha variant	1 OBS	Serious (observational)	Not assessed	Serious (Immuno)	Not assessed	Very Serious	1.3-fold reduction in titers			+ Very Low
10. Any COVID-19 infection, B.1.151/Beta variant	2 OBS	Serious (observational)	Serious	Serious (Immuno)	Not assessed	Very Serious	1.6 to 10-fold reduction in titers			+ Very Low
10. Any COVID-19 infection, B.167.2/Delta lineage	1 OBS	Serious (observational)	Not assessed	Serious (Immuno)	Not assessed	Very Serious	1.4-fold reduction in titers			+ Very Low

Appendix 10. Summary of Findings Table on the Safety of BBIBP-CorV

Safety Outcome		Quality Assessment					Summary of Findings			Certainty
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Overall Assessment	Vaccine [1]	Control [1]	Relative Risk (95%CI)	
1: Solicited adverse reaction	4 RCT[1]	Not serious	Not serious	Not serious	Not serious	Not serious	5595/13464 (41.6%) [a] 5270/13471 (39.1%) [b]	5935/13453 (44.1%)		++++ High
2: Local adverse reaction	4 RCT[1]	Not serious	Not serious	Not serious	Not serious	Not serious	3450/13464 (25.6%) [a] 2786/13471 (20.7%) [b]	3906/13453 (29.9%)		++++ High
3: Systemic adverse reaction	4 RCT[1]	Not serious	Not serious	Not serious	Not serious	Not serious	3695/13464 (27.4%) [a] 3810/13471 (28.3%) [b]	3743/13453 (27.8%)		++++ High
4. Unsolicited adverse event (28d)	4 RCT[1]	Not serious	Not serious	Not serious	Not serious	Not serious	2162/13464 (16.1%) [a] 2094/13464 (15.5%) [b]	2075/13453 (15.4%)		++++ High
5: Serious adverse event	4 RCT[1]	Serious (short ffup)	Not serious	Not serious	Not serious	Not serious	64/13646 (0.5%) [a] 59/13471 (0.4%) [b]	78/13453 (0.6%)	0.83 [a] 0.67 [b]	+++ Moderate

Safety Outcome		Quality Assessment					Summary of Findings			Certainty
		Risk of Bias	Inconsistency	Indirectness	Imprecision	Overall Assessment	Vaccine [1]	Control [1]	Relative Risk (95%CI)	
6: Related serious adverse event (All medically attended adverse events (MAAEs)	4 RCT[1]	Serious (short ffup)	Not serious	Not serious	Not serious	Not serious	0/13646 [a] 2/13471 [b]	0/13453	Not evaluable	Not assessed
7: Withdrawals due to adverse event	4 RCT[1]	Not reported	Not reported	Not reported	Not reported	Not reported	na	na	na	Not assessed
8: Death	4 RCT[1]	Serious (short ffup)	Not serious	Not serious	Not serious	Not serious	No events	No events	No events	No events

1 – values from the Phase 3 trials only (eTable 5, eTable 7 AllKaabi) a – WIV04/WIBP b – HBO2/BiBP c – unspecified strain

Appendix 11. Ongoing Trials Registered at the Clinicaltrials.gov Registry on BBIBP-CorV

NCT Number	Title	Status	Interventions	Outcome Measures	Sponsor/Collaborators	Study Type	Completion Date
NCT04946565	The Impact of Sinopharm COVID-19 Vaccination on Male Fertility	Recruiting	Diagnostic Test: Semen analysis	Sperm density count/ml|Total sperm count per ejaculate|Percentage of motile sperm|Percentage of abnormal sperm forms|Morning serum testosterone	Cairo University	Observational	30-Aug-22
NCT04988048	Collaborative Study to Evaluate Heterologous Vaccination Against Covid-19 in Argentina	Recruiting	Biological: COVID-19 vaccines	Antibody against Spike protein measurement by ELISA test|Incidence of adverse events by measurement of the number of reactions after vaccination|Neutralising Antibody against Spike protein and cellular immune response	Ministry of Public Health, Argentina|Russian Direct Investment Fund	Interventional	15-Feb-22
NCT04984408	Efficacy, Immunogenicity and Safety of BBIBP-CorV Vaccine Against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection.	Not yet recruiting	Biological: BBIBP-CorV - Inactivated SARS-CoV-2 vaccine (Vero cell)|Biological: influenza season quadrivalent Influenza Vaccine (Flu Quadrivalent)	Protection conferred by BBIBP-CorV vaccine against any COVID-19 disease|Incidence of solicited adverse events, unsolicited adverse events and serious adverse events and adverse events of special interest (AESIs)|Protection conferred by BBIBP-CorV vaccine against symptomatic COVID-19 disease|Protection conferred by BBIBP-CorV vaccine against asymptomatic SARS-CoV-2 infection (any SARS-CoV-2 variant)|Protection conferred by BBIBP-CorV vaccine against severe COVID-19 disease and COVID-19 associated death|Geometric Mean Titers (GMT) and Geometric Mean Fold Rise (GMFR) of anti-SARS-CoV-2 neutralizing antibody in subset of participants|Incidence of solicited adverse events, unsolicited adverse events and serious adverse events and adverse events of special interest (AESIs) in HIV-infected adults|Geometric Mean Titers (GMT) and	International Vaccine Institute	Interventional	30-Sep-24

				Geometric Mean Fold Rise (GMFR) of anti-SARS-CoV-2 neutralizing antibody in subset of participants in HIV-infected adults|SARS-CoV-2 sequence variants among HIV-infected and HIV-uninfected, BBIBP-CorV vaccine and placebo recipients|Geometric Mean Titers (GMT) and Geometric Mean Fold Rise (GMFR) of anti-SARS-CoV-2 neutralizing antibody in the Arm 3 as compared to Arm 1 and 2 (subset participants).|Incidence of adverse event (AE) after each vaccination, serious adverse event (SAE), adverse events of special interests (AESIs) according to Brighton Collaboration list for COVID-19 vaccine studies among participants receiving the study vaccines.|Humoral and cellular immune responses of HIV-infected participants as compared to HIV-uninfected vaccine and control arms (subset participants of Arms 1 and 2)|Geometric Mean Titers (GMT) and Geometric Mean Fold Rise (GMFR) of anti-SARS-CoV-2 neutralizing antibody following booster dose of BBIBP-CorV vaccine|Incidence of solicited adverse events, unsolicited adverse events and serious adverse events and adverse events of special interest (AESIs) among HIV uninfected adults.			
NCT04885764	Profiling Antibody Status and Vaccine Effectiveness in Post Vaccination With SARS CoV2 in Ain Shams University	Recruiting	Biological: Astrazeneca/Oxford Vaccine|Biological: Sinopharm vaccine	Short-term effectiveness	Ain Shams University	Interventional	1-Dec-21

					Royal College of Surgeons in Ireland - Medical University of Bahrain|The National Taskforce for Combatting COVID-19-Kingdom of Bahrain|Bahrain Defence Force Royal Medical Services|Ministry of Health, Bahrain|Bahrain International Exhibition & Convention Centre		
NCT04993560	Safety and Efficacy of COVID-19 Prime-boost Vaccine in Bahrain	Completed	Biological: BBIBP-CorV|Biological: BNT162b2	Change from Baseline Immunogenicity at 8 weeks|Reactogenicity		Observational	19-Oct-21
NCT04729374	COVID-19 Vaccine Induced Adaptive Immune Responses	Recruiting		Concentration of anti-SARS-CoV-2 neutralizing antibody in serum|Concentration of serum anti-SARS-CoV-2 binding antibody|Rate of anti-SARS-CoV-2 T cell response|The rate of SARS-CoV-2 infection|Rate of anti-SARS-CoV-2 B cell response	The Affiliated Nanjing Drum Tower Hospital of Nanjing University Medical School	Observational	31-Dec-23

NCT04834869	COVID-19 Vaccines Safety Tracking (CoVaST)	Recruiting	Biological: BNT162b2|Biological: mRNA-1273|Biological: AZD1222|Biological: CoronaVac|Biological: Sinopharm|Biological: Gam-COVID-Vac|Biological: JNJ-78436735|Biological: CVnCoV|Biological: NVX-CoV2373|Biological: BBV152	Local Side Effects|Systemic Side Effects|Unrecognized Side Effects	Masaryk University	Observational	31-Jan-22
NCT04998240	Mix and Match Heterologous Prime-Boost Study Using Approved COVID-19 Vaccines in Mozambique	Not yet recruiting	Biological: BBIBP-CorV - Inactivated SARS-CoV-2 vaccine (Vero cell)|Biological: AZD1222 (replication-deficient Ad type 5 vector expressing full-length spike protein)	Geometric Mean Titers (GMTs) of anti-SARS-CoV-2 neutralizing antibodies|Incidence of SAEs and AESI observed at any time point during the entire study period|Incidence of solicited reactions within 7 days (local reactions) and 14 days (systemic reactions)|Incidence of unsolicited adverse events that are within 28 days after each vaccination|Incidence of changes in laboratory safety measures from baseline to day 28 after each vaccination|Geometric Mean Titers (GMTs) and Geometric Mean Fold Rise (GMFR)	International Vaccine Institute|The Coalition for Epidemic Preparedness Innovations (CEPI)|Instituto Nacional de SaÃºde (INS), Mozambique|University of Antananarivo|Internatio	Interventional	30-Oct-22

					nal Centre for Diarrhoeal Disease Research, Bangladesh |Harvard University|Heidelberg University		