BBIBP-CorV (Covilo)

Post-authorization Studies

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27-Jan-2022

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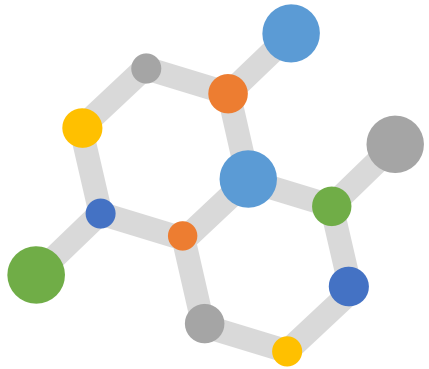
01 Phase III Clinical Study Design

Study Objectives

- Vaccine Efficacy
- Safety
- Immunogenicity



Study Design

- Immunization Schedule: 0-21/28 days
- Vaccine 1: Vaccine 2: Placebo = 1: 1: 1
- Randomized, Double-blind, placebo controlled

Diagnosis Criteria

- Symptom 2A + 1B + PCR positive
- For 48 hours
- Endpoint Outcome Were Collected 14 days after 2nd Dose

UAE, Bahrain, Jordan, Egypt, etc.

Studies on Post-authorization VE

- **Durability of Protection in Phase III Clinical Studies**
- **Phase III Vaccine Efficacy after Booster Dose**
- **Real-world Vaccine Effectiveness**

01 Phase III Clinical Study - Vaccine Efficacy

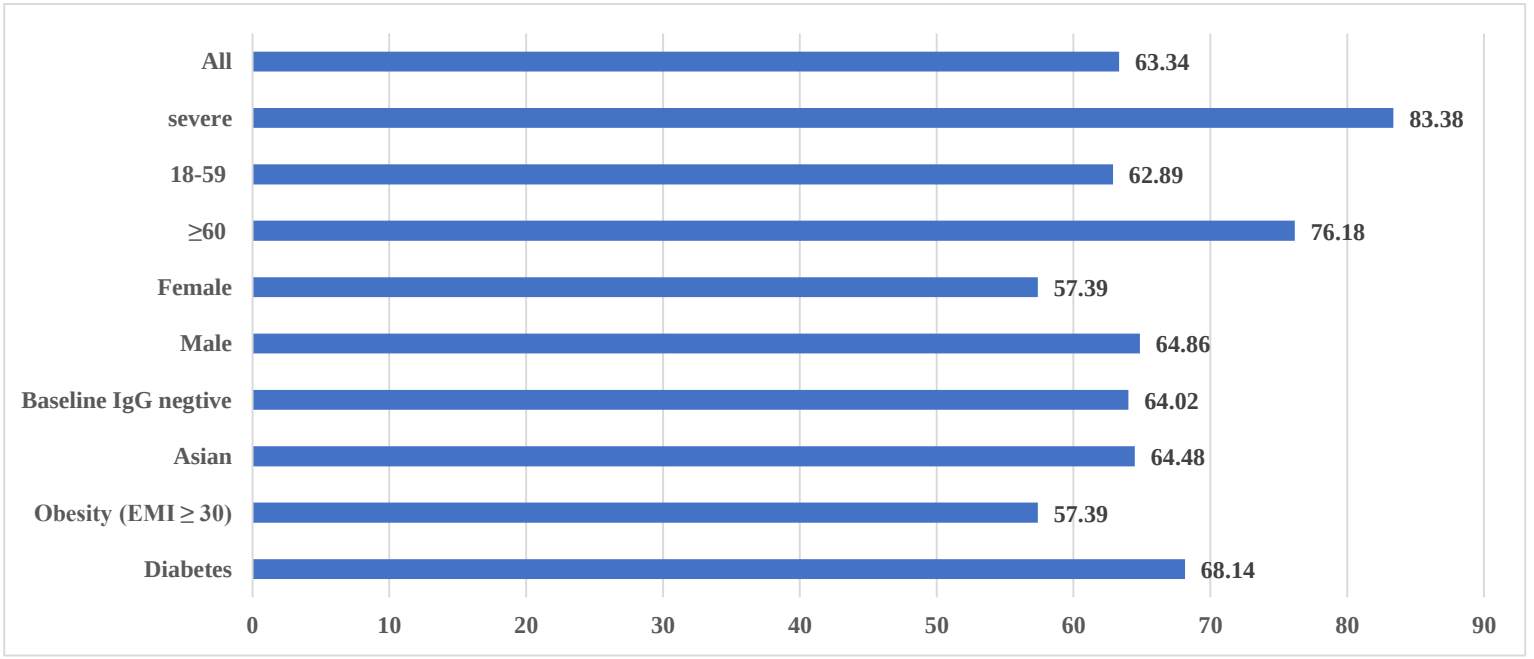
- **In this study, four analyses were carried out at different time points according to the protocol. The vaccine efficacy (VE) in the first analysis was 79.34% (median follow-up time 50 days). The VE in the second analysis was 78.89% (median follow-up time was 112 days). The VE in the final analysis was 63.34% (median follow-up time was 154 days), and the VE in the duarbility protection analysis was 56.87% (median follow-up time was 213 days).**
- **BBIBP-CorV (Covilo) has good efficacy and durable protection.**

Analysis	Cut-off Date	Median Follow-up Time	Vaccine Efficacy (VE)				
			Total VE	Severe illness	Death	18-59 years	≥60 years
Final Analysis	Jan.1st, 2021	154 days	63.34% (54.72, 70.32)	83.38% (-36.99,99.64)		62.89% (54.15, 69.96)	76.18 (48.44, 89.00)
Durability of Protection	Mar. 31st, 2021	213 days	56.87% (50.11, 62.72)	90.05 (59.04, 98.87)	100.00 (-, 100.00)	56.49% (49.62, 62.42)	79.85% (5.46, 97.85)

01 Phase III Clinical Study – Vaccine Efficacy in Different Subgroups

➢ **BBIBP-CorV (Covilo) has good efficacy in different subgroups and patients with comorbidities**

VE Analysis in different subgroups based on person-year incidence (mFAS1)

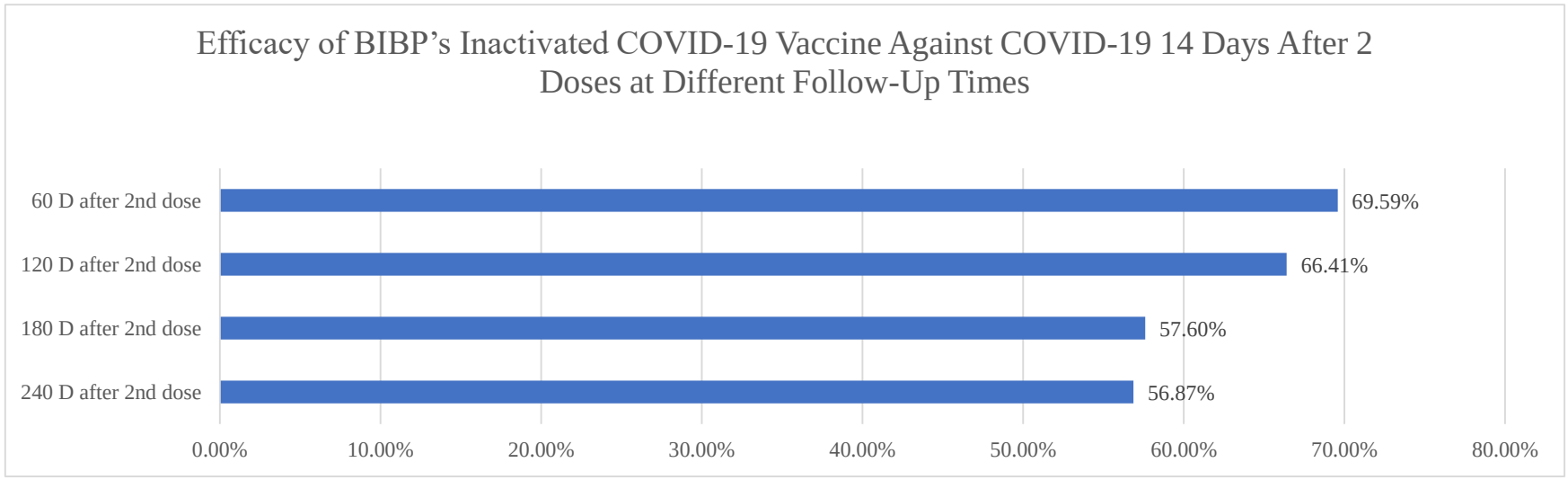


01 Phase III Clinical Study - Vaccine Efficacy at Different Follow-up Times

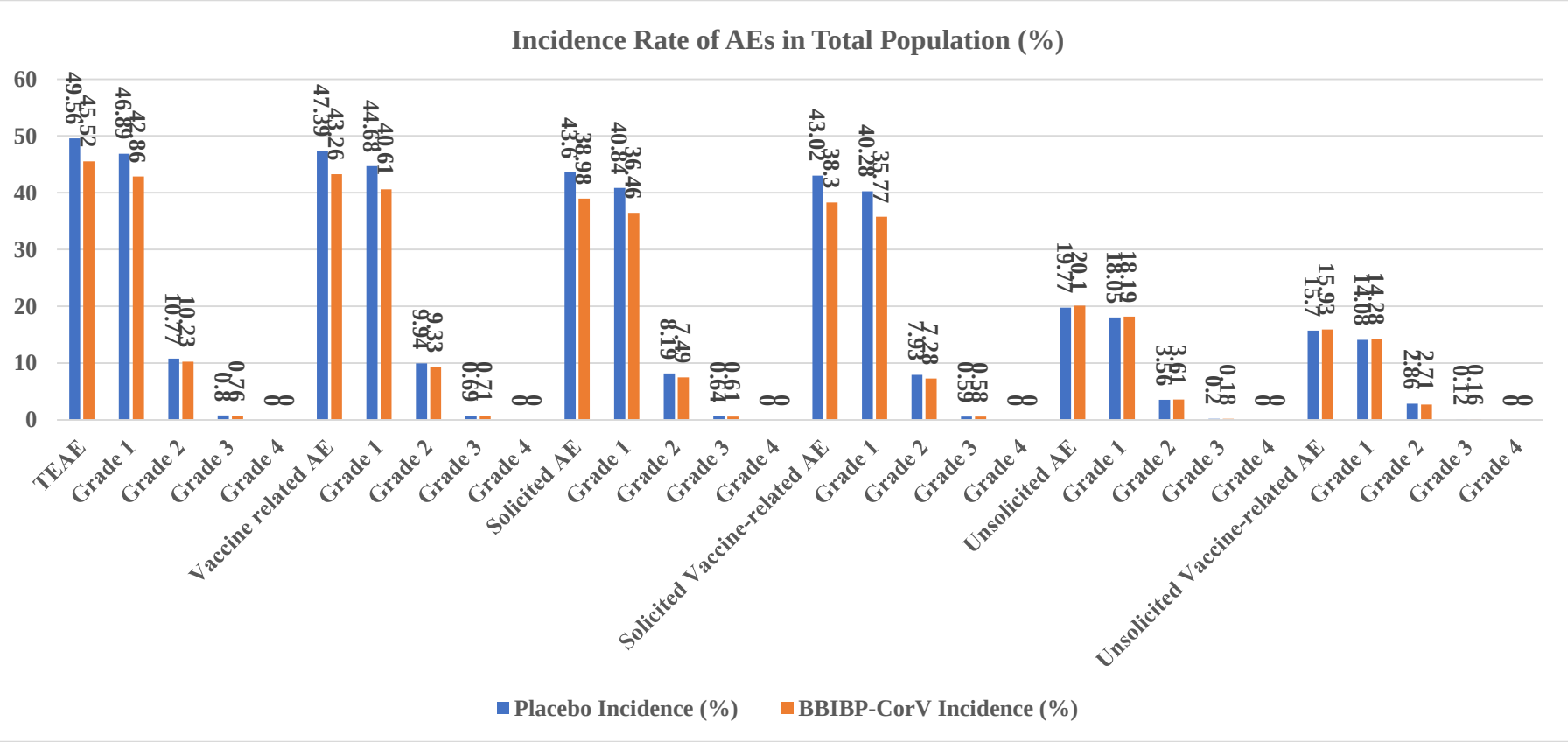
- **The VE at 60 days, 120 days, 180 days and 240 days after full immunization were analyzed.**

  The VE against COVID-19 were 69.59%, 66.41%, 57.60% and 56.87%, respectively.

- **BBIBP-CorV (Covilo) has good efficacy up to 240 days after the 2nd dose**

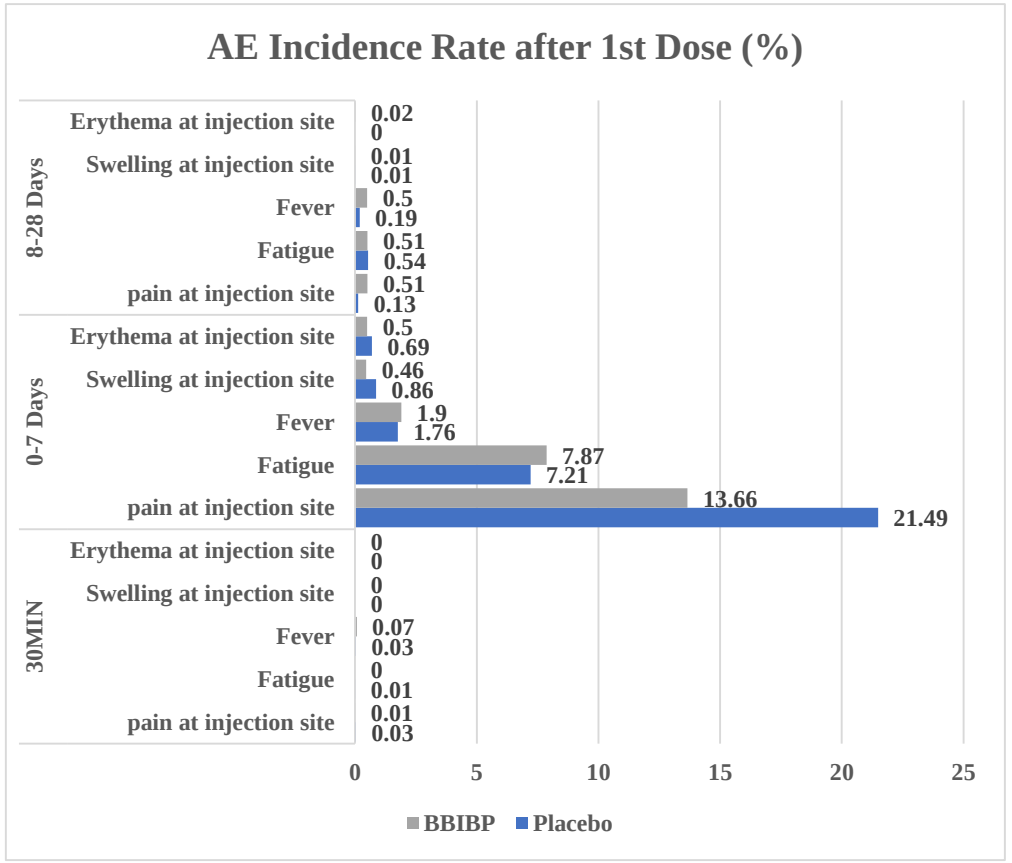


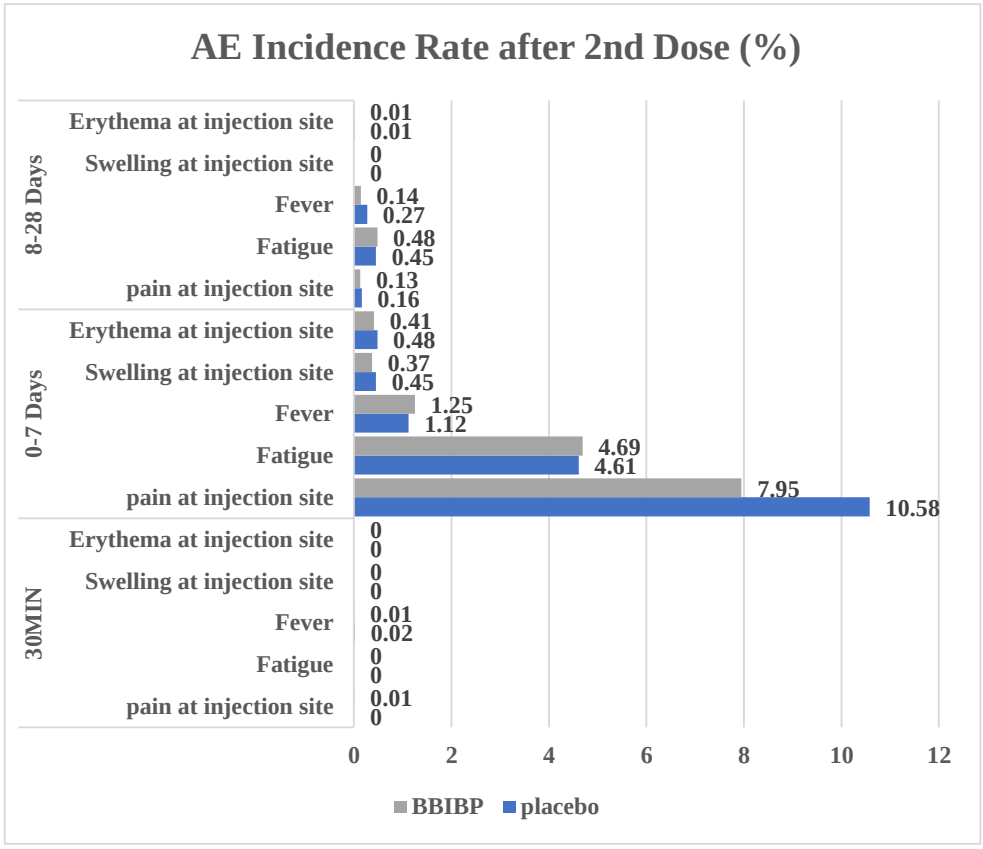
01 Phase III Clinical Study - Safety



- **The overall incidence of adverse events were 49.56% in the placebo group and 45.52% in the BBIBP-CorV (Covilo) group.**
- **The incidence of AE in the placebo group was higher than those in the vaccine group, and the difference between the groups was statistically significant.**
- **Majority of adverse reaction was rated Grade 1**

01 Phase III Clinical Study - Safety



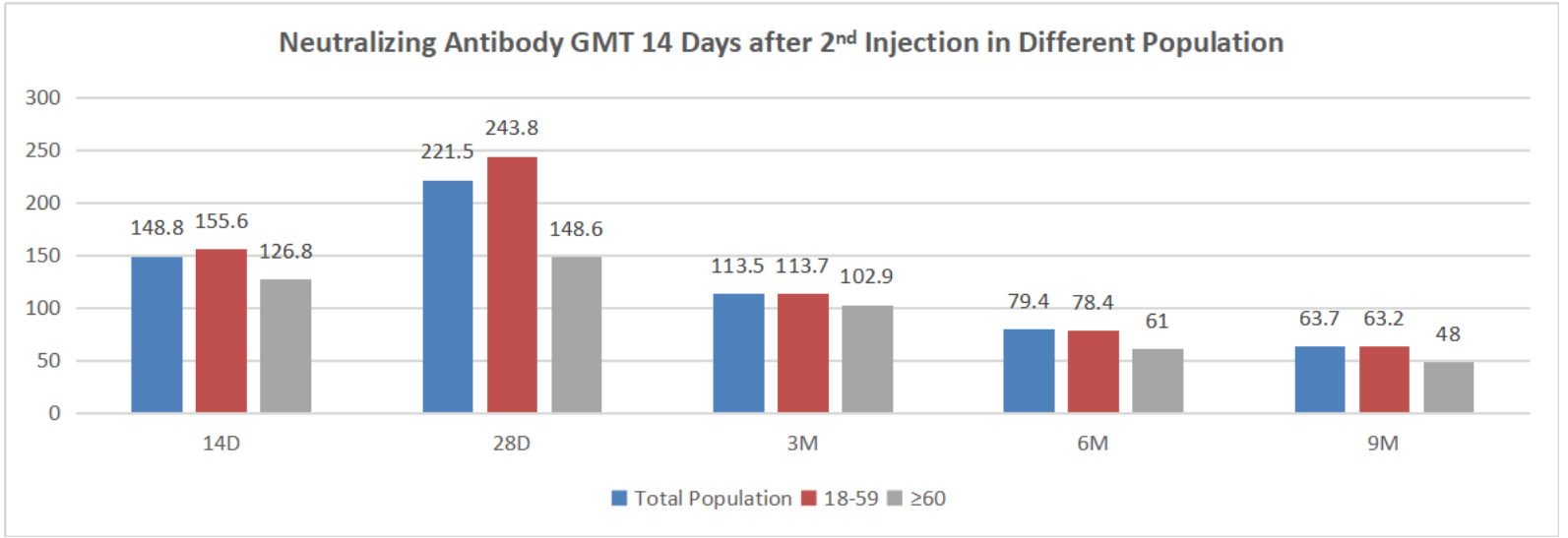


- **Majority of the AEs after each dose are pain at injection site;**
- **Occurence of AEs are condensed within 0-7 days after each immunizaiton.**

01 Phase III Clinical Study - Immunogenicity

14 days, 28 days, 3M, 6M, 9M after 2nd dose:

- **Antibody seroconversion rate in total population was 99%;**
- **The GMT of anti-SARS-CoV-2 neutralizing antibody of BBIBP-CorV (Covilo) in the total population was 148.8, 215.5, 113.5, 79.4 and 63.7, respectively.**
- **The GMT in the 18-59 population was higher than that of ≥60. The GMT in the vaccine groups were significantly higher than the placebo group.**



Studies on Post-authorization VE

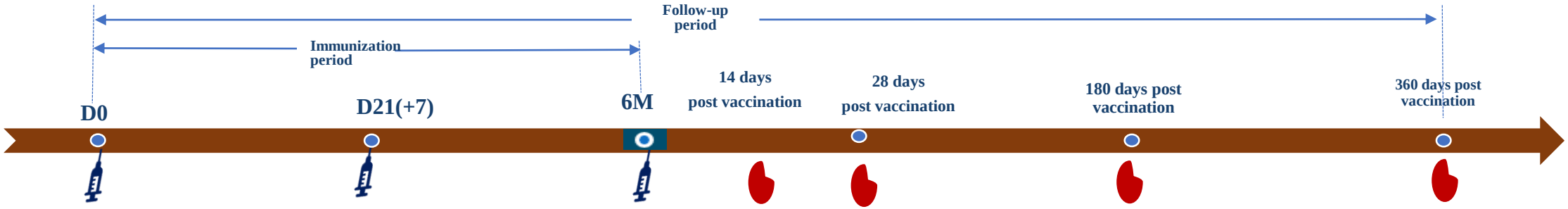
- Durability of Protection in Phase III Clinical Studies
- **Phase III VE after Booster Dose**
- Real-world Vaccine Effectiveness

03 Phase III VE after Booster Dose

- **Booster immunization:**

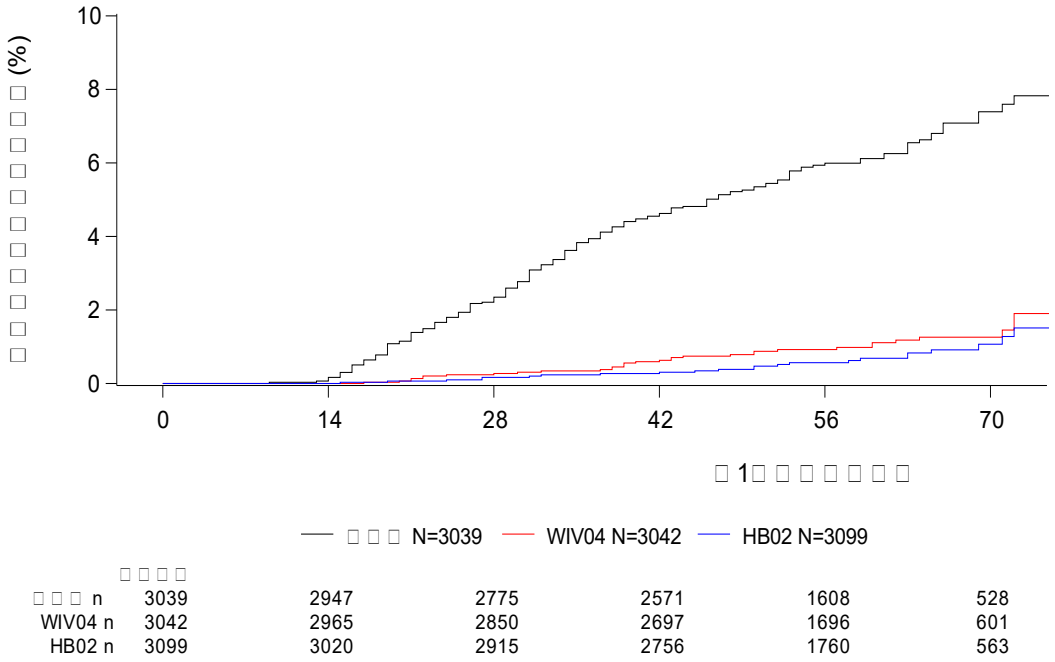
  -Maintain the original protocol, maintain the blindness for booster immunization;

  - BBIBP-CorV (Covilo) group and placebo group were vaccinated with booster dose according to the original grouping
- **A 3rd dose was administered 6 months following the 2nd dose;**
- **Immunization schedule: 0, 21(+7) days, ≥6M**
- **Population: ≥18 years;**
- **A total of 9,370 participants entered the stage of booster immunization, among which 9,309 participants completed the whole schedule of booster immunization (placebo: 3,076, WIBP: 3,083, BIBP: 3,150), the participants came from 93 countries and regions and balanced across the groups.**



03 Phase III VE after Booster Dose

- **The total VE against COVID-19 is 86.3%; The VE against severe case was 94.09%.**
- **VE after a booster dose was increased by 30% compared with the VE after 2 doses (56.87%, 213 days).**



n	3039	2947	2775	2571	1608	528
WIV04 n	3042	2965	2850	2697	1696	601
HB02 n	3099	3020	2915	2756	1760	563

Total VE: 86.3%

95%CI(79.56%, 91.13%);

VE against severe cases: 94.09%;

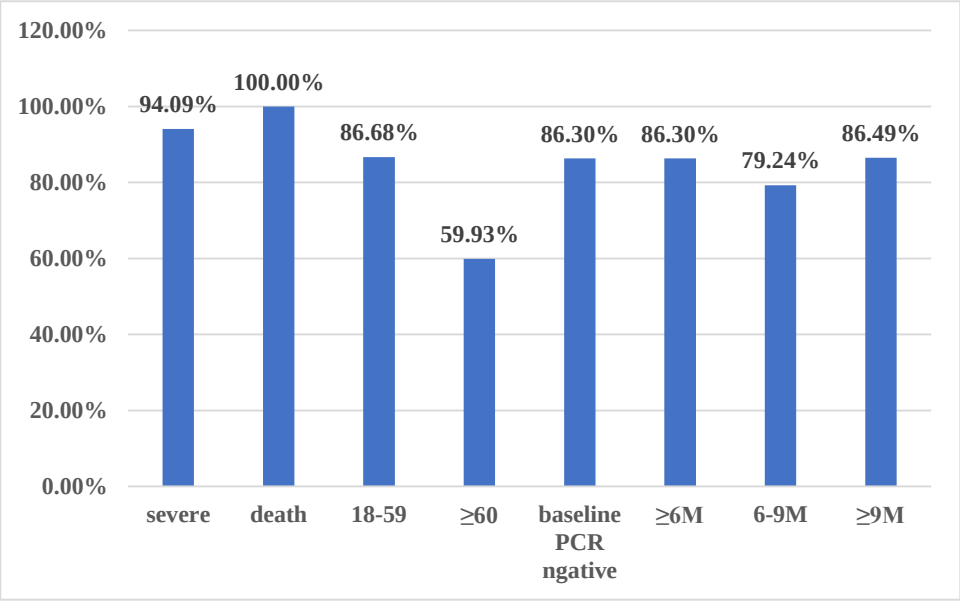
95%CI(61.95%, 99.86%);

VE against deaths: 100%;

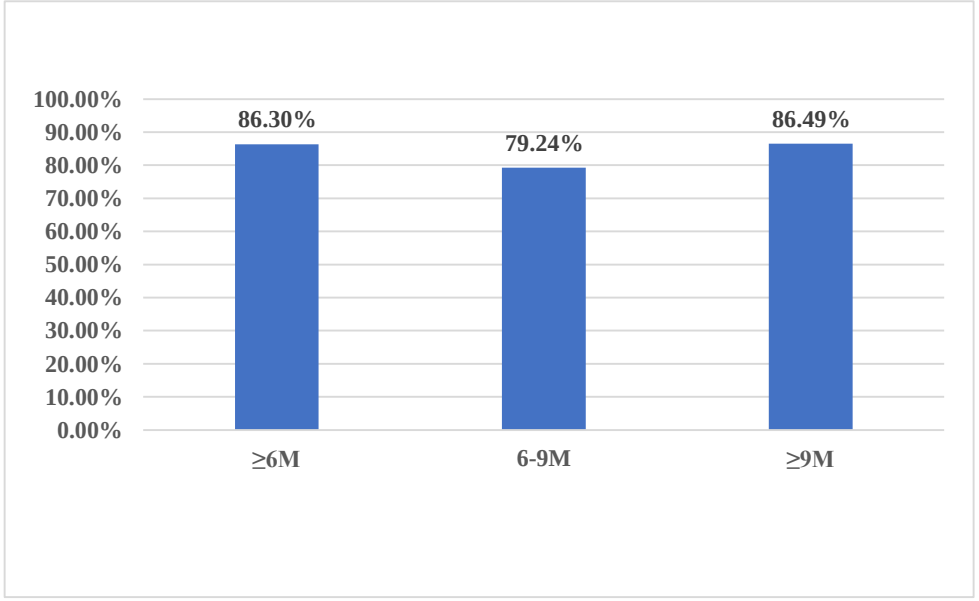
03 Phase III VE after Booster Dose

- BBIBP-CorV (Covilo) showed good vaccine efficacy in different subpopulations. Except for subgroup aged ≥ 60, VEs in other groups were all above 80%;
- Total VE after a booster dose given at ≥6M interval following the primary 2-dose series was 86.30%, and the VE after a booster given at interval of 6-9M and ≥9M was 79.24% and 86.49%, respectively;
- **BBIBP-CorV (Covilo) shows good efficacy with 1 booster ≥ 6 months after 2 doses of primary series.**

BBIBP-CorV (Covilo) VE in Different Subgroups

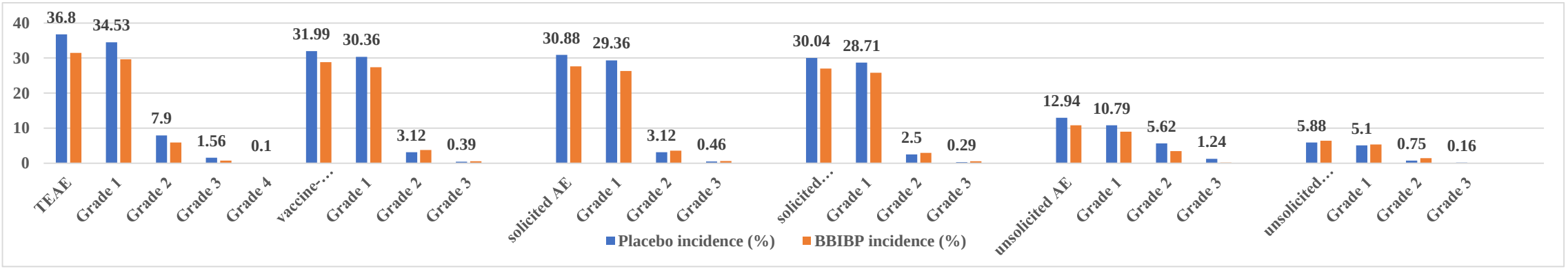


BBIBP-CorV (Covilo) VE after 1 booster dose at Different Time Interval

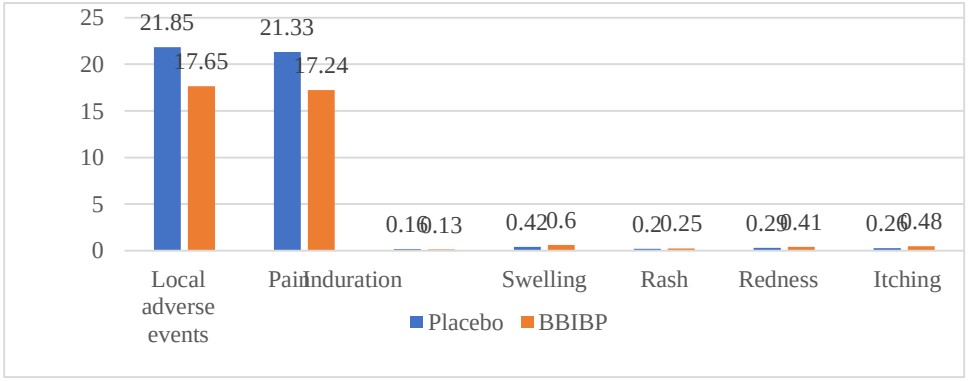


03 Booster Dose - Safety

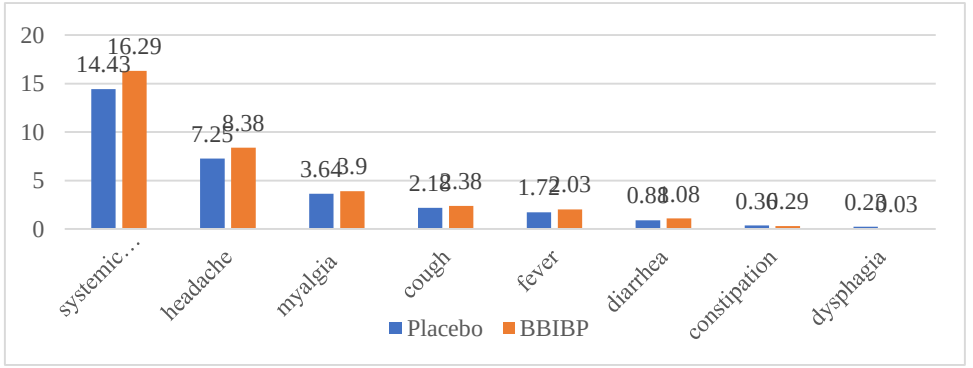
Adverse Events after Booster Dose in Total Population



Local Adverse Events after Booster Dose



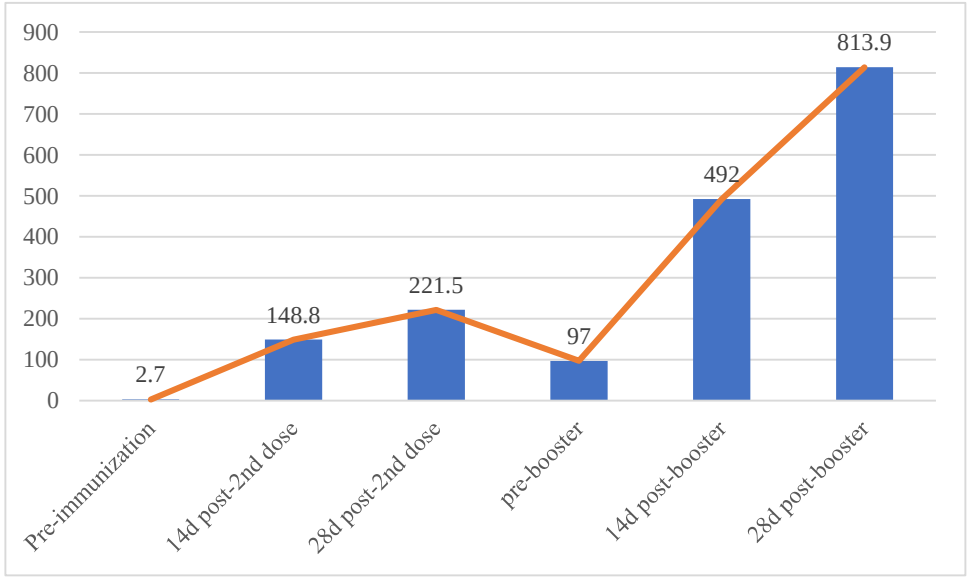
Systemic Adverse Events after Booster Dose



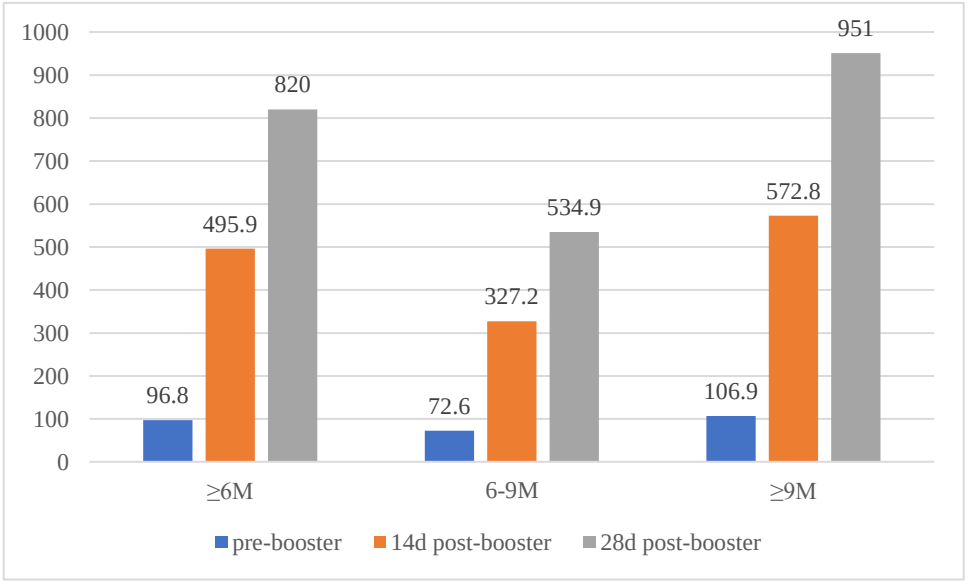
- **The adverse events after the booster dose were less than that after 2nd dose, and most of AEs were grade 1 events, and there were no adverse events above grade 4;**
- **The local adverse events were mainly pain after the booster dose, , and the systemic adverse events were mainly headache, myalgia and cough**

03 Booster Dose – Antibody Level

GMT after 1 booster dose



Neutralizing antibody GMT after 1 booster dose at different interval



- **Participants over 18 years old received 1 booster dose (≥6M after 2nd dose), and neutralizing antibody GMT increased significantly;**
- **Compared with GMT before the booster dose, neutralizing antibody GMT after booster immunization increased by 10 folds**

Studies on Post-authorization VE

- Durability of Protection in Phase III Clinical Studies
- Phase III VE of Booster Dose
- **Real-world Vaccine Effectiveness**

02 Real-world Vaccine Effectiveness

BBIBP-CorV (Covilo) was significantly effective in preventing severe illness and death

Countries/Regions	Results
Sri Lanka	Positive seroconversion rate: 95%
The Seychelles	Against death: 97.64%, against infection: 76%
Victoria Falls, Zimbabwe	Death cases dropped to 0
Mongolia	Against death: 96%
Nanjing, China	Against severe case caused by Delta variant: 88%
Guangdong, China	Against moderate case: 70.2%, against severe case: 100%
Peru	Death case dropped by 98%
Argentina	Against death in >60 years: 84%, good safety profile in 3-11 years

02 Real-world Vaccine Effectiveness - Argentina

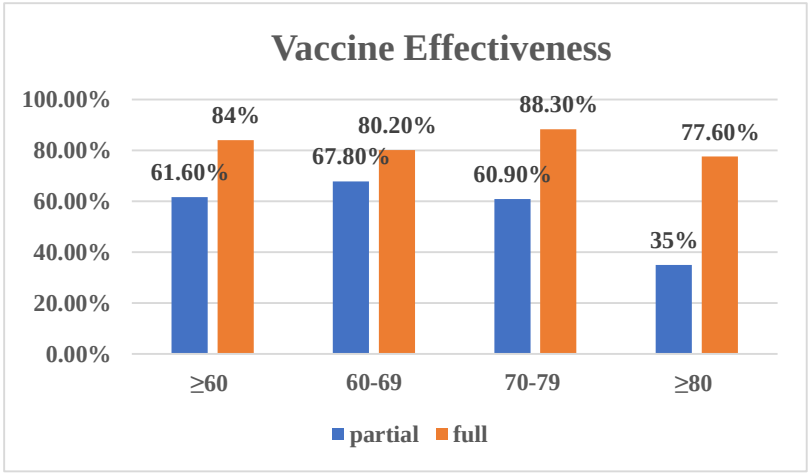
VE Evaluation

- **Method: Retrospective test negative design (TND) observational study**
- **Population: Elderly population (≥ 60 years old)**
- **Sample size: 147,908 participants**
- **Data Collection Time: January 1, 2021.1-June 22, 2021.6.**
- **VE results: The VE in preventing COVID-19 death after two doses of vaccination was 84%.**

VE of BBIBP-CorV (Covilo) against COVID-19 death in population over 60 years old

Vaccination Status	VE (95% CI)			
	≥ 60 years N=147,908	60-69 yrs N=87,281	70-79 years N=40, 669	80 years N=19,958
1 dose	61.6% (55.9%%-6.2%)	67.8% (61.5%-73.5%)	60.9%(51.6%–67.6%)	35% (10.0%-54.0%)
2 doses	84% (77.9%-88.0%)	80.2%(67.5%–88.4%)	88.3% (80.1%-93.1%)	77.6%(60.0%%–87.5%)

Source Estudio Efectividad De CampaÑa Nacional De VacunaciÓn En ReducciÓn De La Mortalidad Por Covid-19 En Personas De 60 AÑos Y Mayores. Argentina,30 de junio de 2021.

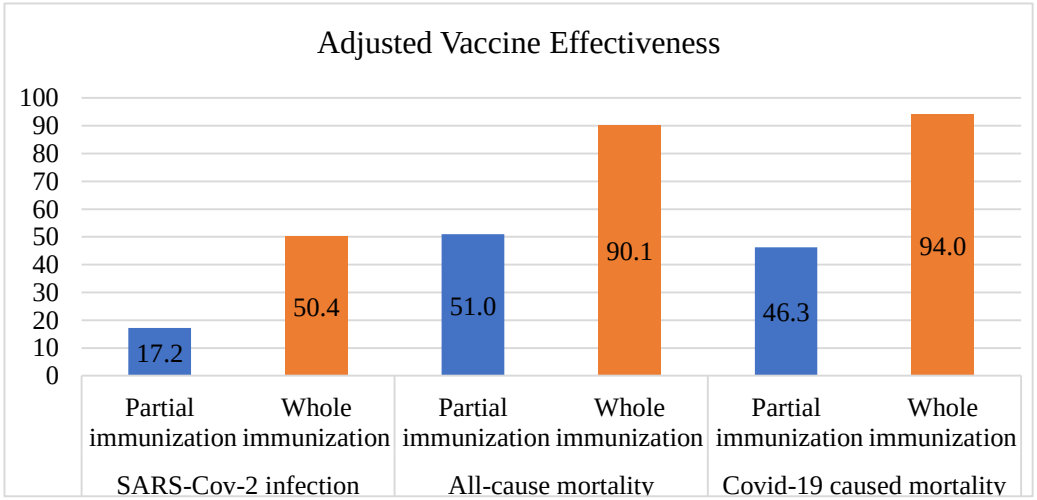


02 Real-world Vaccine Effectiveness-Peru

VE Evaluation:

- **Method: Retrospective test negative design (TND) observational study.**
- **Population: Healthcare workers (HCW), ≥ 18 years old.**
- **Data Collection Time: Feb 9, 2021 - June 30, 2021.**
- **Sample size: 606,870 participants.**
- **Results: VE after full immunization against all-caused death was 90.1%, and VE against COVID-19 caused death was 94.0%.**

Outcome	HR/IRR	IC 95%	VE(1-HR)x100
SARS-CoV-2 infection			
Partial immunization	0.83	0.80-0.85	17.20%
Full immunization	0.5	0.48-0.51	50.40%
All-cause mortality			
Partial unification	0.49	0.39-0.62	51%
Complete unification	0.1	0.08-0.13	90.10%
COVID-19 caused morality			
Partial immunization	0.54	0.41-0.70	46.30%
Full immunization	0.06	0.04-0.09	94.00%



Source: Efectvividad de la vacuna BBIBP-CorV para prevenir infeccion y muerte en personal de salud

02 Real-world Vaccine Effectiveness - Sri Lanka

◆ BBIBP-CorV (Covilo) has a good efficacy against COVID-19 caused deaths

Vaccination Status	Population	Outcome	Number of people	Number of deaths	VE
Vaccinated (1 dose)	Total Population	SARS-CoV-2 caused deaths	10,820,941	651	94.3%
Vaccinated (2 doses)			8,875,888	200	97.9%
Unvaccinated			8,269,747	8,796	-

◆ Immunogenicity

After healthy participants in Sri Lankan were vaccinated with BBIBP-CorV (Covilo), 95% of them were seroconverted, and the vaccine induced similar levels of antibody to B.1.617.2 natural infection.

◆ Breakthrough infection

Vaccination status	Population	Outcome	Number	Total infection rate (number)	Severe infection rate (number)	Total mortality (number)
Vaccinated (1 dose)	Healthcare Worker	Breakthrough infection	129	11.63% (15)	1.55% (2)	0 (0)
Vaccinated (2 doses)			129	10.85% (14)	0 (0)	0 (0)
Unvaccinated			18	22.22% (4)	0 (0)	11.11% (2)

02 Real-world Vaccine Effectiveness - UAE

Study I

- **Method: A retrospective cohort study**
- **Data Collection Time: September 01, 2020 - May 1, 2021;**
- **Population: PCR positive cohort**
- **Results: Among the population with positive SARS-CoV-2 PCR test reults, based on the incidence rates, the VE in fully vaccinated individuals was 80%, 92%, and 97% in preventing COVID-19 related hospitalization, ICU admissions, and deaths.**

Outcome	Fully vaccinated	Unvaccinated
Hospitalization		
No. of participants	62931	91941
No. of incident cases	622	3909
Vaccine Effectiveness (95% CI),%	79.8 (78-81.4)	/
ICU Admission		
No. of participants	62931	91941
No. of incident cases	55	909
Vaccine Effectiveness (95% CI),%	92.2 (89.7-94.1)	/
Deaths		
No. of participants	62931	91941
No. of incident cases	1	45
Vaccine Effectiveness (95% CI),%	97.1 (83-99.9)	/

02 Real-world Vaccine Effectiveness - UAE

Study II

- **Method: Prospective cohort study**
- **Data Collection Time: September 14th, 2020 - December 21st 2020**
- **Population: 11,322 individuals who received the two-dose BBIBP-CorV (Covilo) (Frontliners)**
- **Results: The safety was good. The seroconversion rate was high 14 days after two doses of vaccination. The infection rates at 90 days and 120 days after vaccination was 0.72% and 0.97%, respectively.**

Characteristics	Negative/Asymtomatic (n-11, 228) n (%)	SARS-COV-2 positive (n- 94) n (%)	Total (n-11,322) n (%)
Age category			
< 50 years	9,716 (86.53%)	84 (89.36%)	9,800 (86.56%)
≥ 50 years	1,512 (13.47%)	10 (10.64%)	1,522 (13.44%)
Gender			
Male	9,227 (82.18%)	70 (74.47%)	9,297 (82.11%)
Female	2,001 (17.82%)	24 (25.53%)	2,025 (17.89%)
Comorbidities			
Any comorbidity	1,054 (9.39%)	15 (15.96%)	1,069 (9.44%)
Diabetic, N (%)	442 (3.94%)	9 (9.57%)	451 (3.98%)
Hypertension	617 (5.50%)	9 (9.57%)	626 (5.53%)
Cancer	109 (0.97%)	0 (0.00%)	109 (0.96%)
Pulmonary Diseases	20 (0.18%)	0 (0.00%)	20 (0.18%)
Immunosuppression	9 (0.08%)	0 (0.00%)	9 (0.08%)
Transplant	3 (0.03%)	0 (0.00%)	3 (0.03%)
Other comorbidities	183 (1.63%)	3 (3.19%)	186 (1.64%)

02 Real-world Vaccine Effectiveness - Hungary

- **Method**

  Retrospective, observational study

- **Population**

  ≥ 16 years

  895,465 persons vaccinated using BBIBP-CorV (Covilo)

- **Data Collection Time**

  January 22 - June 10, 2021

- **Results**

1. Seven days after second dose of vaccination, the effectiveness of vaccine in preventing symptomatic SARS-CoV-2 infection was 68.7%; The sensitivity analysis of ≥ 14 days and ≥ 28 days the second dose yielded similar results;
2. The effectiveness of vaccine against COVID-19-related death was 87.8%. Sensitivity analysis of ≥ 14 days and ≥ 28 days after second dose yielded similar results

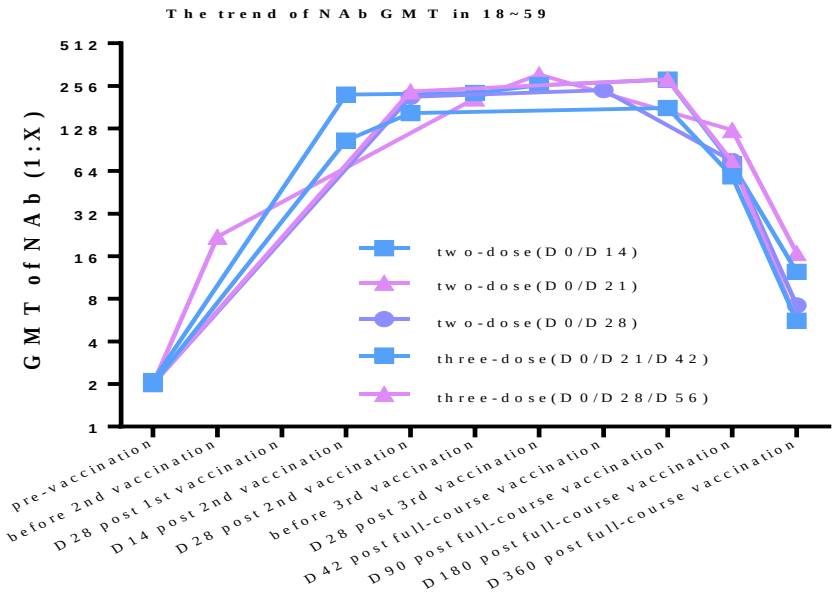
Effectiveness of BBIBP-CorV (Covilo) against Infection and Death

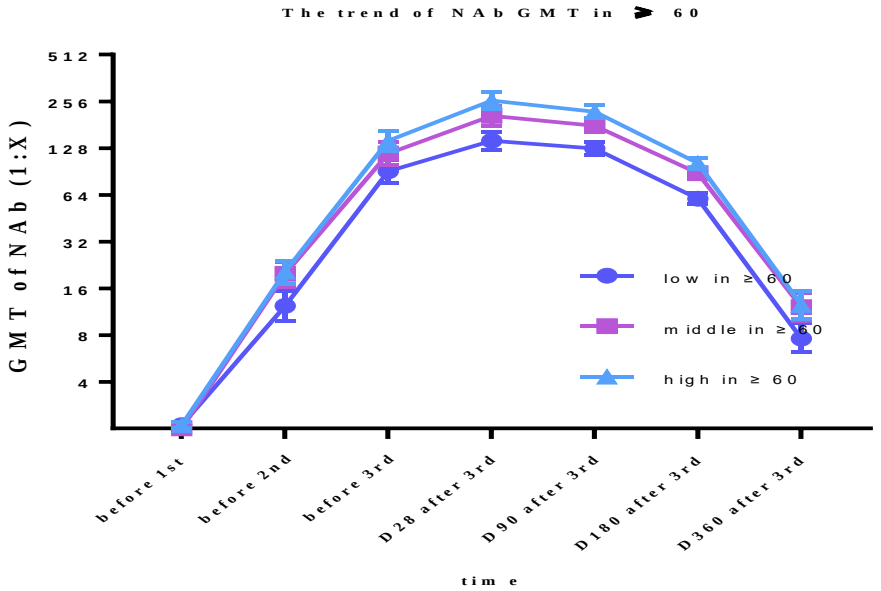
	Vaccinated Persons	SARS-CoV-2 infection	COVID-19-related death
		VE 95% CI	VE 95%CI
7 days after 2nd dose	895, 465	68.7% (67.2%-70.1%)	87.8%(86.1%–89.4%)
14 days after 2nd dose	895, 465	72.8% (71.2%-74.4%)	86.0%%(83.7%%–87.9%)
28 days after 2nd dose	895, 465	74.2% (71.8%-76.5%)	89.2%(86.4%–91.5%)

Immune Persistence and booster schedule finding

- **Phase I/II Immune Persistence Study**
- **Immuno-bridging Clinical Study**

04 Phase I/II Immune Persistence Study - ≥ 18 years





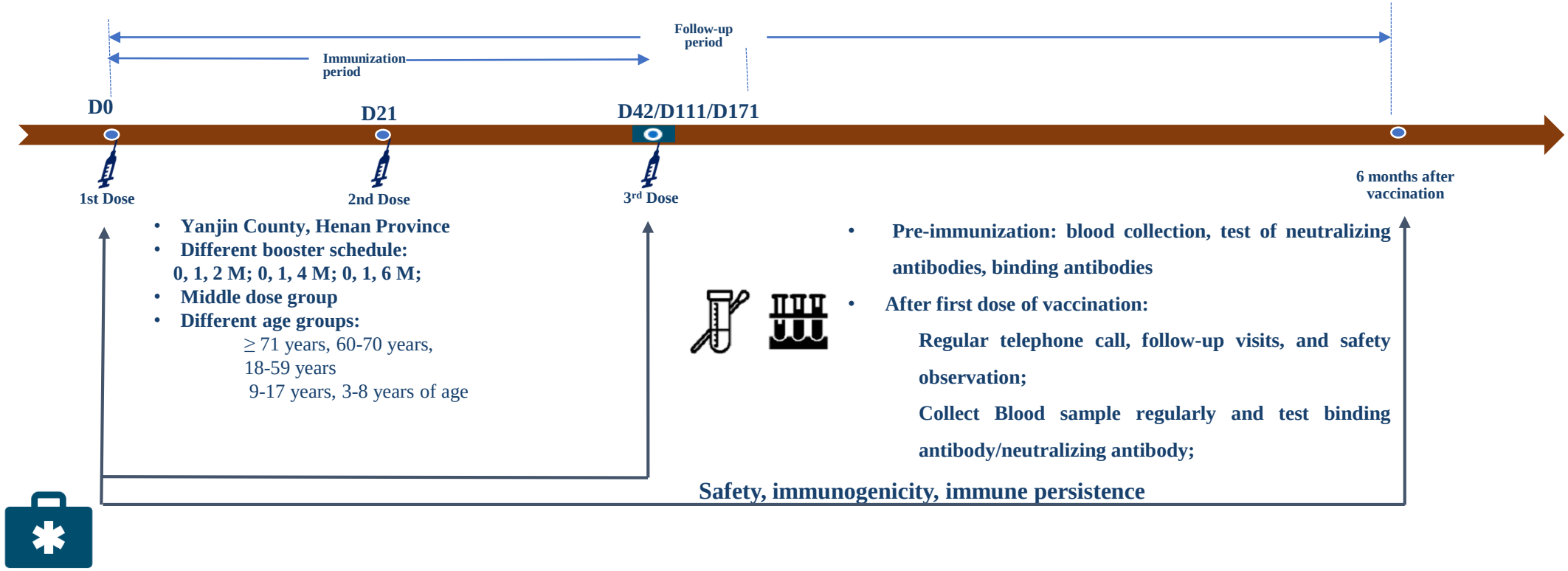
- **In Phase I/II clinical studies, in population over 18 years old, different dosages and immunization schedules were used to evaluate vaccine safety, and to explore immunogenicity**
- **Good immunogenicity was observed in the group aged 18 ~ 59 and the group aged ≥ 60 after vaccination.**
- **The antibody level showed no obvious declining at 90 days after full immunization, and showed significant declining trend after 180 days.**

Immune Persistence and booster timing finding

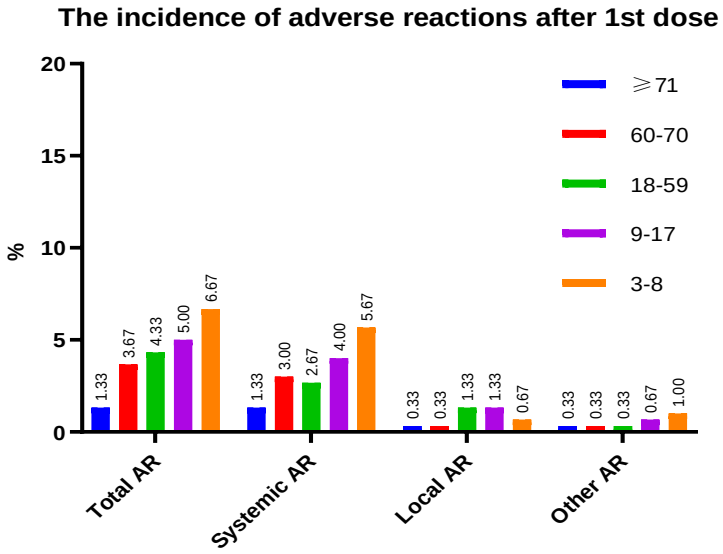
- Phase I/II Immune Persistence Study
- **Immuno-bridging Clinical Study**

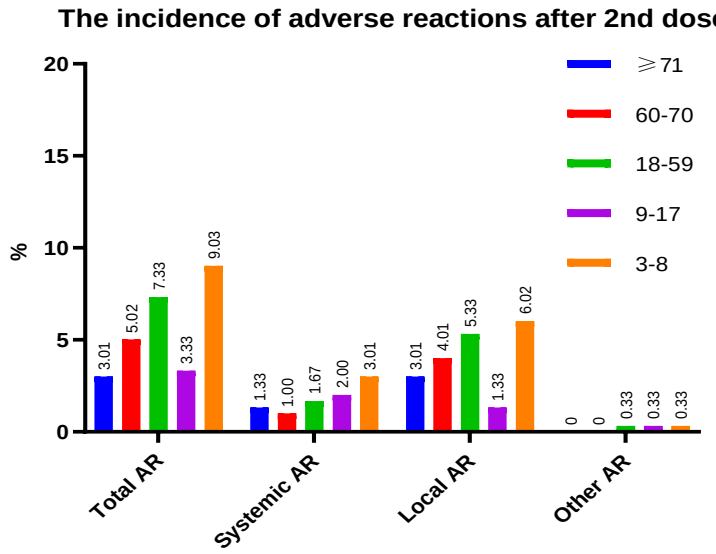
05 Immuno-bridging Clinical Study

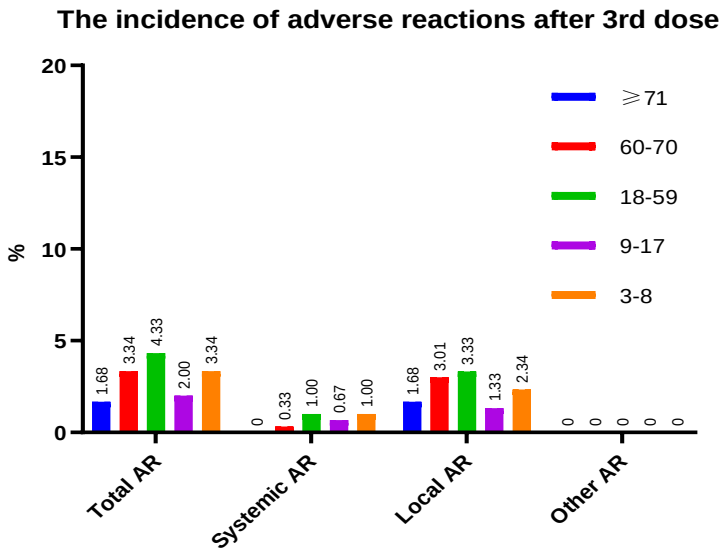
- **To evaluate the immunogenicity and booster schedule among populations aged 3-17, ≥ 60 and aged 18-59**
- **Primary Immunization Schedule: 0, 21 (+7) days;**
- **Booster Dose Schedule: 0, 1 and 2 months; 0, 1, 4 months; 0, 1 and 6 months**



05 Immuno-bridging Clinical Study - Safety

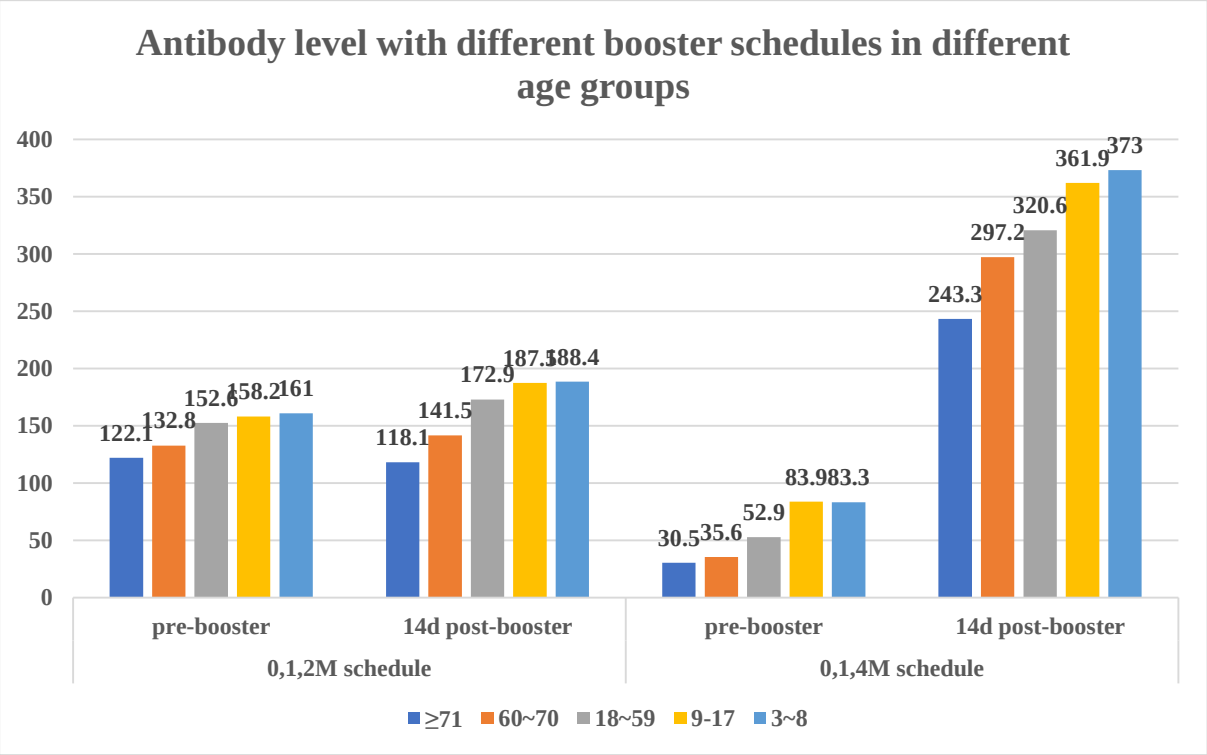






- The total incidence of adverse reactions was low across 4,400 subjects of all ages,.
- Local adverse reactions were mainly pain, and systemic adverse reactions were mainly fever.
- Most of adverse reactions occurred within 7 days after vaccination and were mainly grade 1 and 2. The incidence of adverse reactions were not observed increasing with the number of dose.

05 Immune-bridging Clinical Study - booster schedule finding



- According to the current available data, a booster dose given at 4 months after the primary dose can induce significant higher antibody titer in all age groups compared to booster dose given at 2 months, suggesting a longer interval of the booster dose can result a better boosting effect across all ages.
- Serums at 0,1,6M schedule is currently under testing.

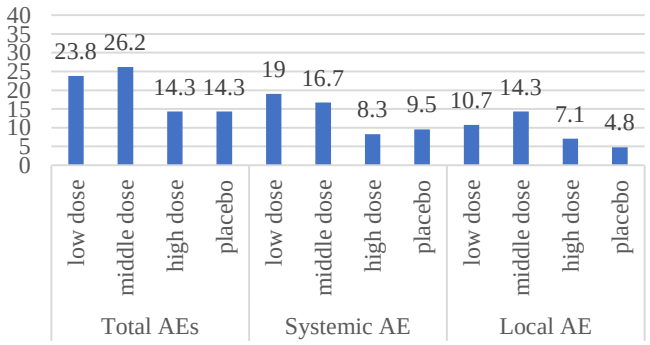
Studies in Population Aged 3-17

- **Phase I/II Study of Immune Persistence**
- **Post-authorization Safety Evaluation**

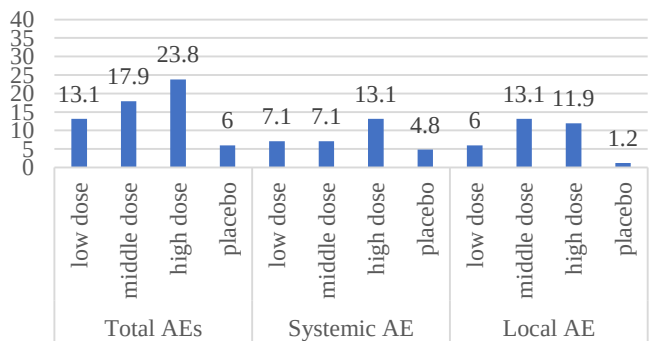
06 Phase I/II Study - Safety

- **Site: Shangqiu City, Henan Province**
- **Immunization schedule: 0, 28, 56 days**

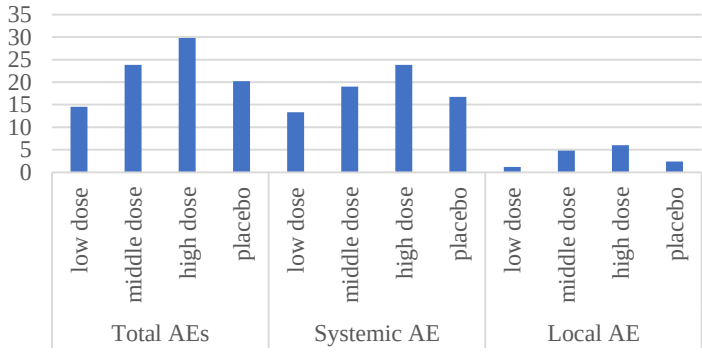
Total AEs in 13 to 17



Total AEs in 6 to 12



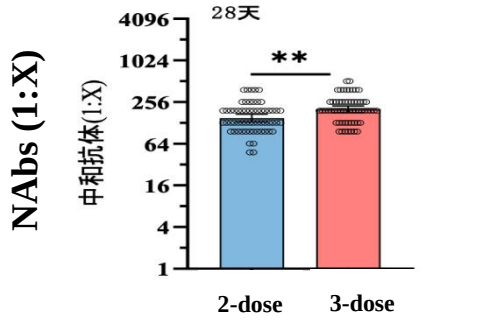
Total AEs in 3 to 5

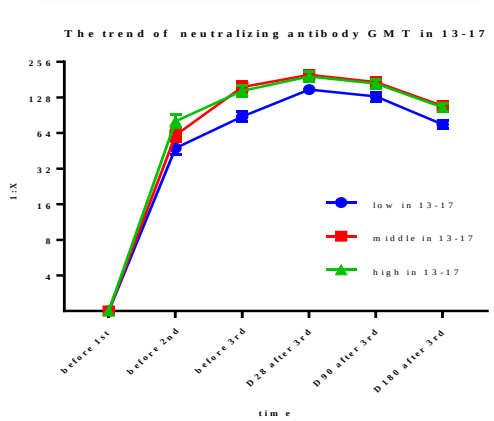


- **Good safety in population 3-17 years of age;**
- **Local adverse reactions were mainly pain at the injection site (incidence rate of 6-12%);**
- **The main systemic adverse reactions were fever (the incidence rate was 7-23%).**

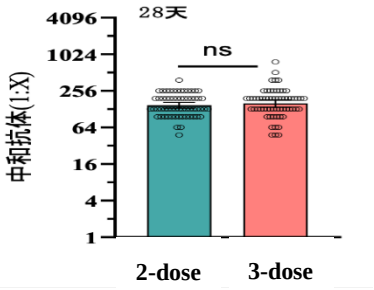
06 Phase I/II Clinical Study - Immune Persistence

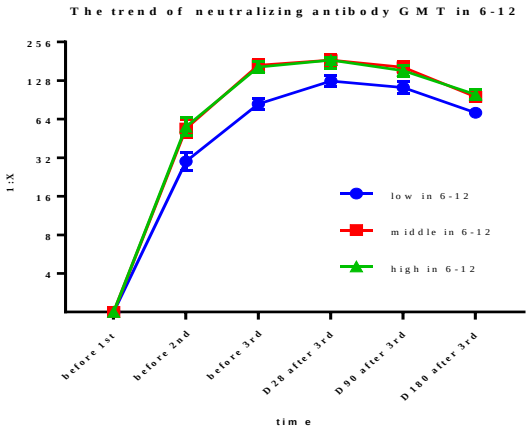
13-17 years old



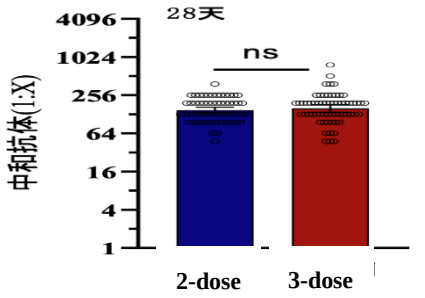


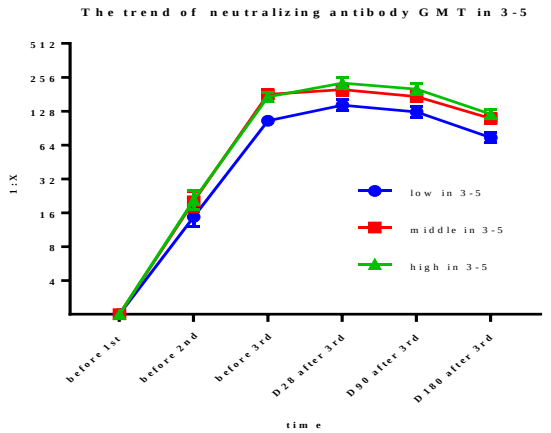
6-12 years old





3-5 years old





- **The post-immunization antibody level in population aged 3-5, 6-12 and 13-17 increased with the increased of doses.**
- **The antibody GMT at 90 days after full immunization was slightly lower than that at 28 days, but still maintained a relatively high level.**
- **The antibody GMT showed declining trend at 180 days after full immunization which was consistent to adults.**

Studies in Population Aged 3-17

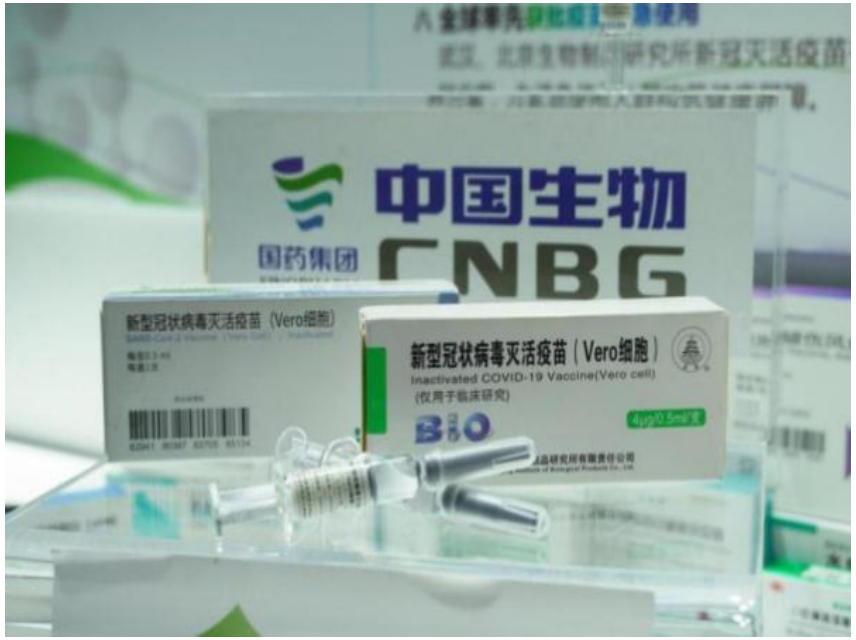
- Phase I/II Study of Immune Persistence
- **Post-authorization Safety Evaluation**

06 3-17 Cohort - Safety

- **Emergency use in population aged 3-17 was approved in China on July 16th , 2021; As of November 7th , 2021, 106,907,914 doses of BBIBP-CorV (Covilo) had been used in population aged 3-17 with good safety.**
- **Common reaction (as per symptoms): the incidence rate of common reactions among population aged 3-17 is 6.050/100,000 doses, of which the incidence rate of local reaction was 0.564/100,000 and the incidence rate of systemic reaction was 5.486/100,000;**
- **The incidence rate of abnormal reactions in population aged 3-17 was 0.618/100,000 doses, of which the incidence rate of non-severe abnormal reactions was 0.530/100,000 doses, and the incidence rate of severe abnormal reactions was 0.088/100,000 doses.**
- **Most of the adverse reactions occurred within 48 hours of vaccination.**

09 3-17 Cohort- Approval Status

- **China:** July 16th , 2021, BBIBP-CorV (Covilo) has been approved for emergency use among people aged 3-17
- **United Arab Emirates:** August 2nd , 2021, the Ministry of Health of the United Arab Emirates announced approval of the BBIBP-CorV (Covilo) for use in population aged 3-17;
- **Bahrain**: August 17th , 2021, the Vaccination Committee of the Ministry of Health of Bahrain approved for use in people aged 3-17.
- **Argentina:** October 1st , 2021, Argentina approved children aged 3-11 to be vaccinated with BBIBP-CorV (Covilo)
- **Pakistan, Belarus, Tobago, Trinidad, Morocco:** successively approved emergency use in population aged 3-17

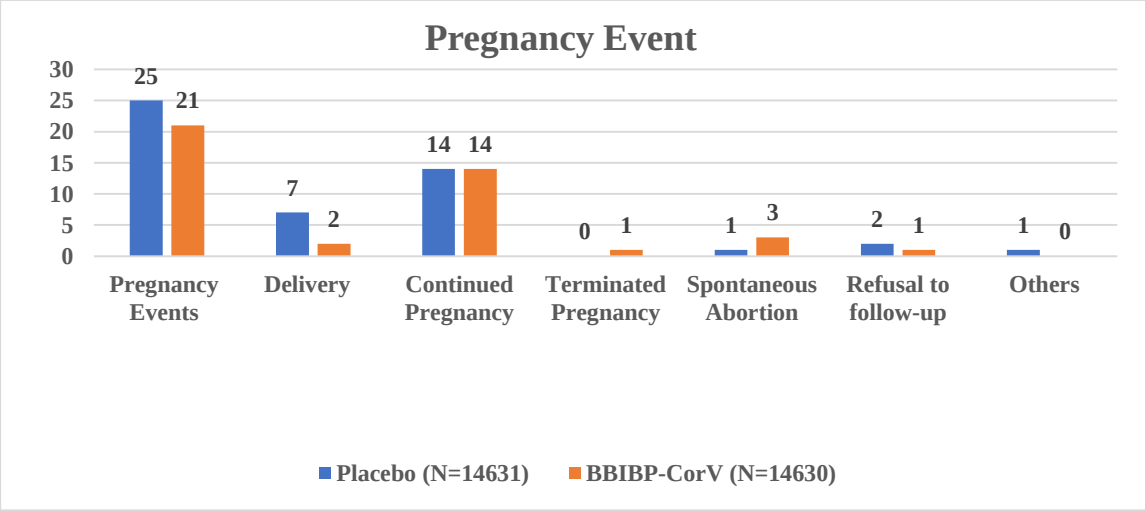


Studies in Special Populations

- Special Population - Pregnant Women
- Special Population – Hypertension & Diabetes

10 Special Population - Pregnant Women

- **As of March 31st, 2021, there were 77 pregnancy events in this Phase III study, of which, 25 were in placebo group and 21 in BBIBP-CorV (Covilo) group.**
- **11 occurred after the first dose and 66 occurred after the second dose.**
- **There were 28 continued pregnancy, 9 delivery (normal newborn), 1 spontaneous termination of pregnancy, 4 spontaneous abortion, 3 participants refused to be followed up. There was no difference between the groups**



11 Special Population – Hypertension & Diabetes

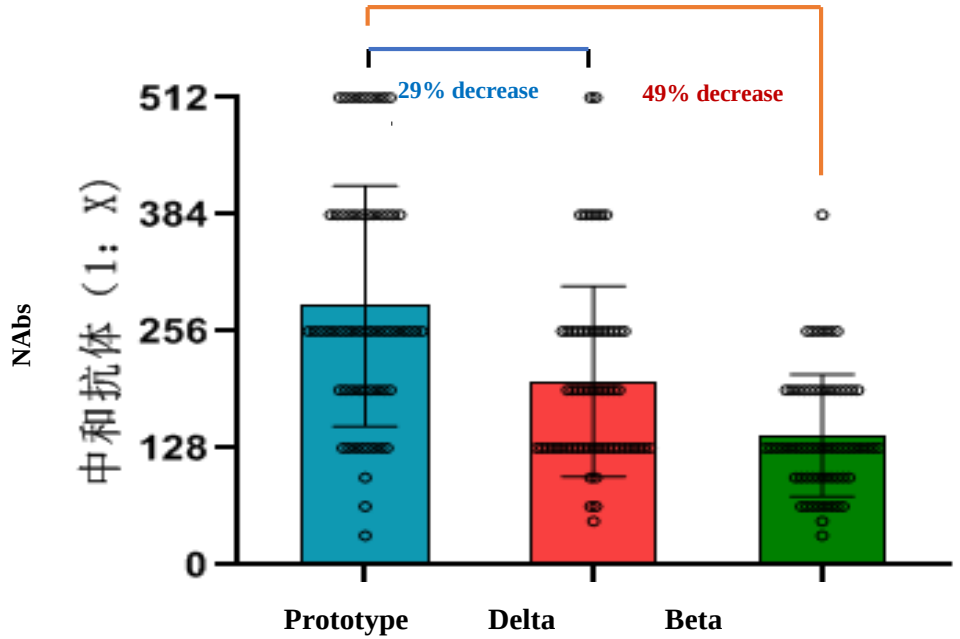
- To evaluate the immunogenicity and safety of BBIBP-CorV (Covilo) after vaccination in population aged 60 and above with hypertension and diabetes.
- Sample size: 480 participants each in hypertension group, diabetes group and healthy control group; planned enrollment: 1,440 participants.
- The seroconversion rate in hypertension group, diabetes group, hypertention+diabetes combined group and healthy control group were all 100%, there's no significant difference in GMT between the groups.
- Good safety after vaccination. The local adverse reactions were mainly pain at injection site. Majority of adverse reactions were dizziness, fatigue and headache.

Cross-neutralization against VOCs

- **Against Delta and Beta Variants**
- **Against Omicron Variant**

12 Cross-neutralization against Different VOCs

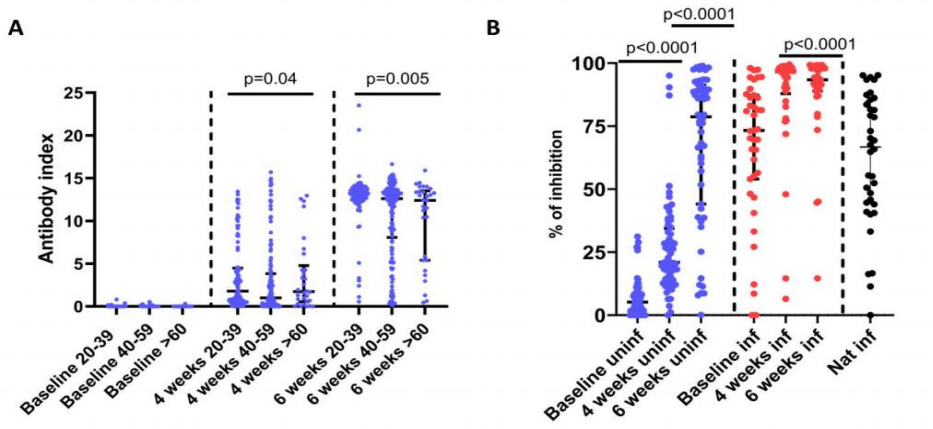
Neutralizing antibody titers 28 days after 2nd dose in middle dose group in Phase II

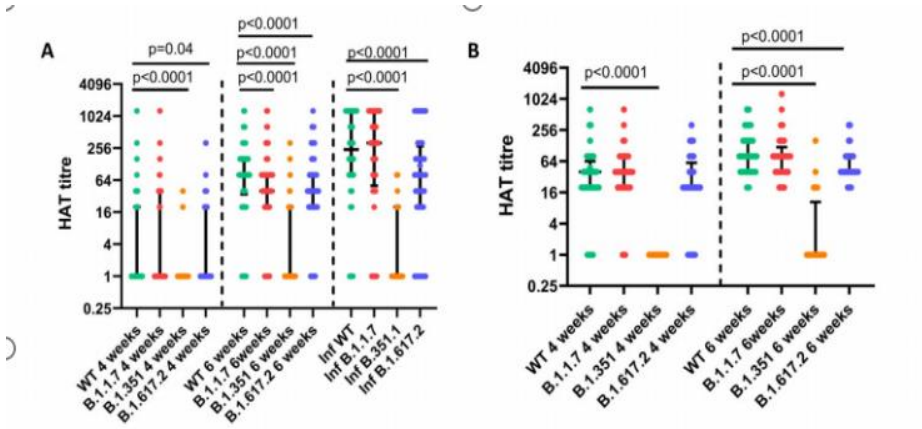


- Sera post 2 doses showed cross-neutralizing effect against both Beta and Delta variants.
- In comparison with the neutralizing antibody titer against the prototype strain, there was slight reduction in the antibody titer against Delta variant, and the extent of reduction against Delta variant was less than that of Beta variant. The vaccine can still confer good protection.

13 Against Delta and Beta Variants - Sri Lanka Study

- **Against VOCs: 1.38-fold reduction in antibody level against Delta variant while a 10-fold reduction was seen against Beta.**





Source: medRxiv preprint doi: https://doi.org/10.1101/2021.07.15.21260621

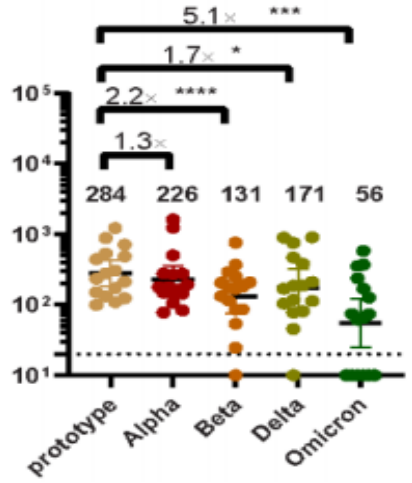
15 Cross-neutralization against Different VOCs

Use Phase III clinical serum to cross-neutralize Delta, Beta and Omicron variants;

For Delta, Beta and Omicron strains, cross-neutralizing capacity after two doses were reduced by 53%, 65% and 64%, respectively, and were reduced by 63%, 75% and 83% after three doses;

Cross-neutralization by using serum after full immunization with inactivated vaccine showed although the neutralizing antibody level against Beta and Delta variants reduced to various degree, but still remained at a certain level.

①



——bioRxiv preprint

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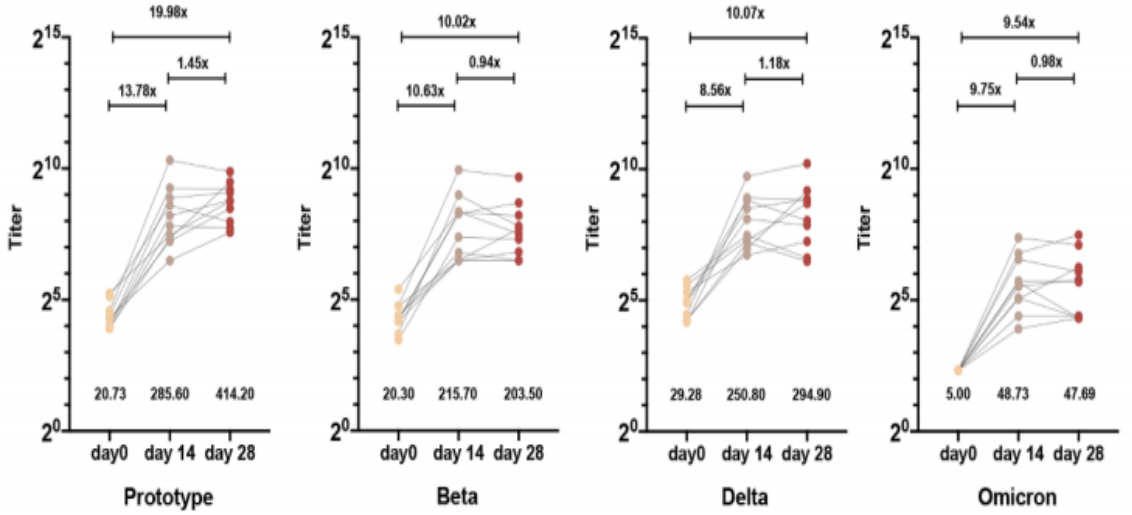

——Emerging Microbes & Infections

Summary

- **Good durability of protection: Phase III clinical results showed that the total vaccine efficacy (median follow-up time 213 days) was 56.87% after 2 doses, 83.38% against severe illness and 100% against deaths;**
- **In real-world use, the results from many countries also demonstrated a good vaccine effectiveness against severe illness and deaths.**
- **After one booster dose at ≥6M after the primary series, the total vaccine efficacy was 86.3%. Compared with pre-booster immunization, the vaccine efficacy was increased by 30%, the vaccine also resulted good safety and 100% seroconversion rate;**
- **The Phase I/II clinical studies in adult and paediatric population all showed declining trend 180 days after full immunization; the immuno-bridging study also showed that immunization schedule of 0,1,4M is superior than 0,1,2M and can produce the better GMT results;**
- **The vaccine had good safety and immunogenicity in population aged 3-17 and special populations;**
- **The vaccine can produce cross-neutralizing response against Delta and Beta variants. Although the antibody against Omicron reduced significantly, there is still some protection.**

Thank you!