COVID-19 Vaccine

(Vero Cell), Inactivated

China National Biotec Group Company Limited

Beijing Institute of Biological Products Co., Ltd.

29 April, 2021

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COVID-19 Vaccine (Vero Cell), Inactivated

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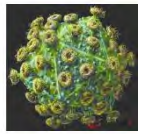
Prevention of COVID-19 caused by SARS-CoV-2

Key Components



Inactivated SARS-CoV-2 virus

Dosage

6.5 U/dose

Adjuvant

Aluminum hydroxide

Packaging

0.5ml/ Pre-filled syringe/vial

Storage and Transportation

2~8℃

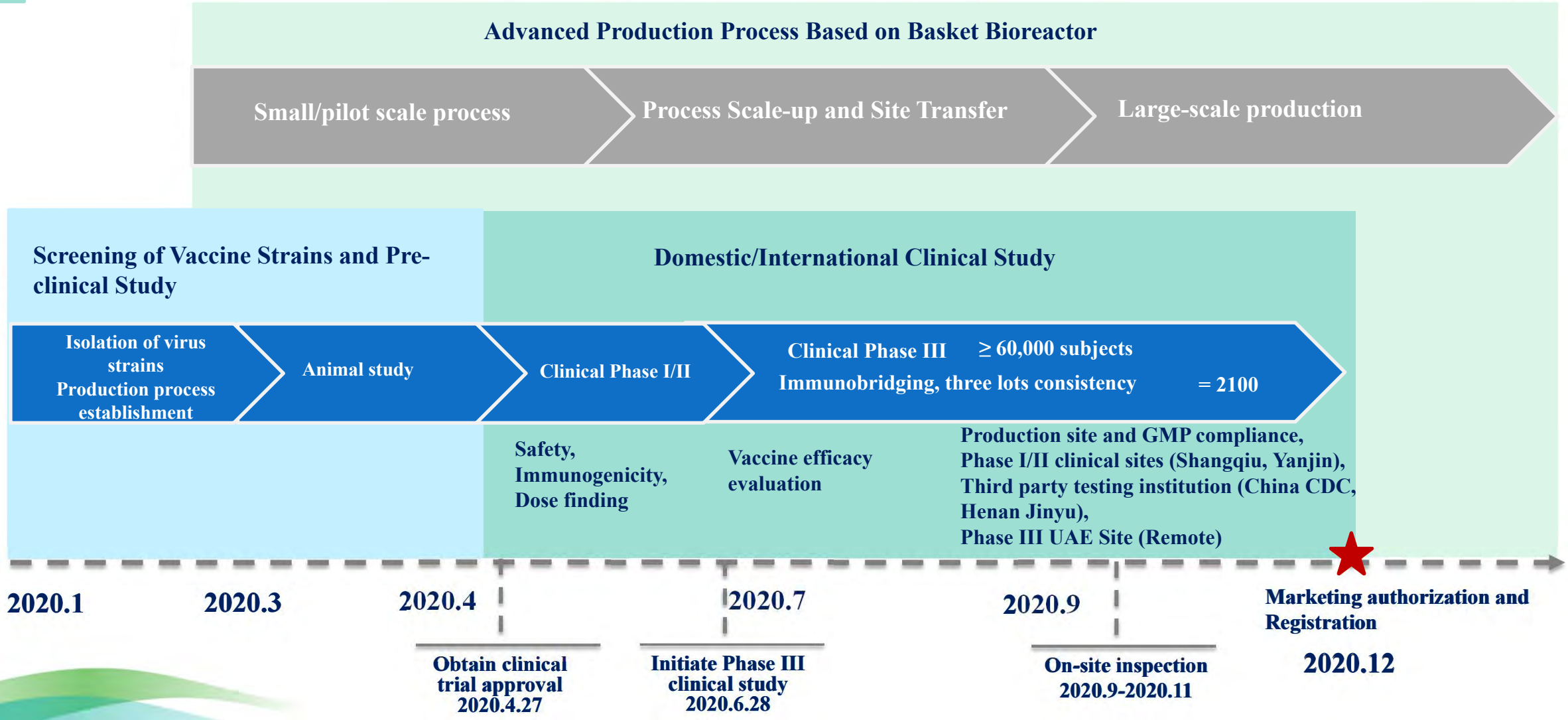
Validity Period

Tentatively 2 years

Applicable population

- 18 years old and above
- Study of the 3-17-year-old cohorts are completed.

Research and Development Process

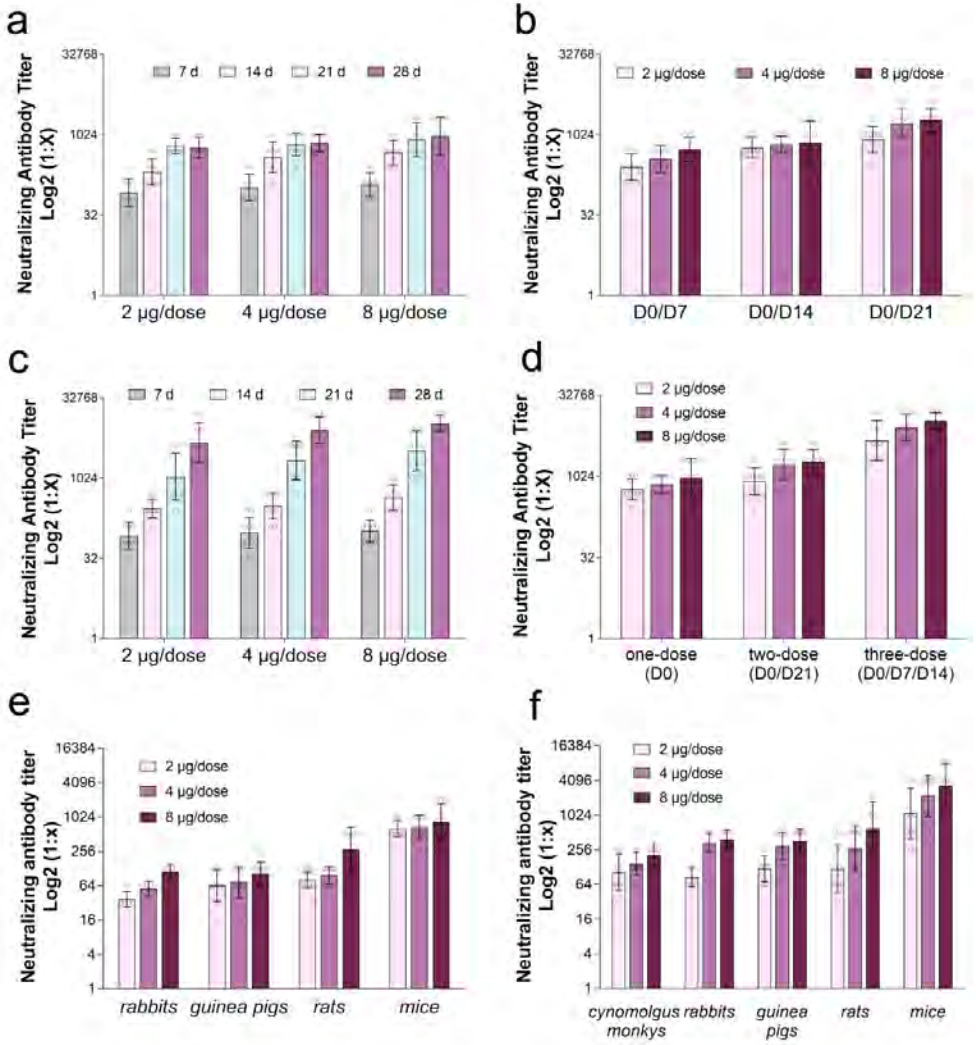


Pre-clinical Study

- Immunogenicity
- Safety
- Challenge study

Immunogenicity

Study Results of Dosage and Immunization Schedules in Various Animal Species



Dosages

All produced high titer antibodies;

Antibody level is positively correlated with time;

The antibody level in the medium and low dose group reached its peak in 21 days;

The high dose group reached the peak in 14 days.

Immunization Schedules

(0/7, 0/14, 0/21) all produced high titer antibodies;

There was a positive correlation between the number of doses and the antibody level;

In the high and medium dose groups, 3 doses are better than 2 doses and 2 doses are better than 1 dose;

0/21 is better than 0/7 and 0/14.

The vaccine showed good immunogenicity in 6 species

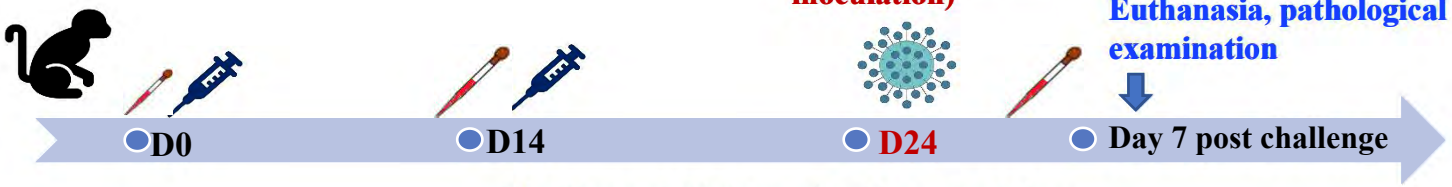
Safety Evaluation (JOINN Lab Report)

The safety evaluation of acute toxicity, long term toxicity, reproductive toxicity and allergy has been completed, and no abnormal reaction has been observed.

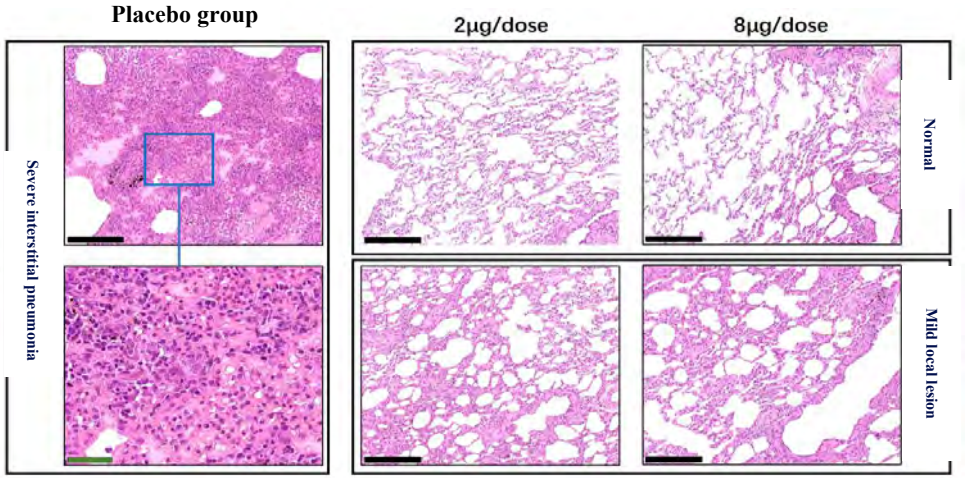
Study Item	Study Animal	Grouping	Route of administration	Time of administration	Result
Acute toxicity	Rat	High, medium dose, control	Intramuscular injection, single administration		No abnormal reaction observed
Reproductive toxicity		2 dose groups, control	Intramuscular injection, Multiple administrations	Male: D1/D15/D29/D43 Female: D1/D15/D29/GD6/PND7	
Long term toxicity	Rat	4 dose groups, control		D1/D15/D29/D43	
	Cynomolgus macaques	3 dose groups, control		D1/D8/D15/D22	
Allergy	Guinea pigs	2 dose groups, control	Sensitize by intramuscular injection, stimulate by intravenous injection		

Challenge Study

Objective: To evaluate the active protection of the inactivated SAS-CoV-2 vaccine in rhesus monkeys and provide animal study data for clinical research.



Challenge at 10 days after the second dose



Group	Pathology	Viral load
High dose group	Mild interstitial pneumonia (4/4)	The viral load was 0 (4/4)
Low dose group	Mild interstitial pneumonia (4/4)	The viral load was 0 (4/4)
Placebo Group	Severe interstitial pneumonia (2/2)	High viral load (2/2)

Study showed that:

- **The inactivated SARS-CoV-2 vaccine has good protective effect and no antibody-dependent enhancement effect (ADE) was observed.**

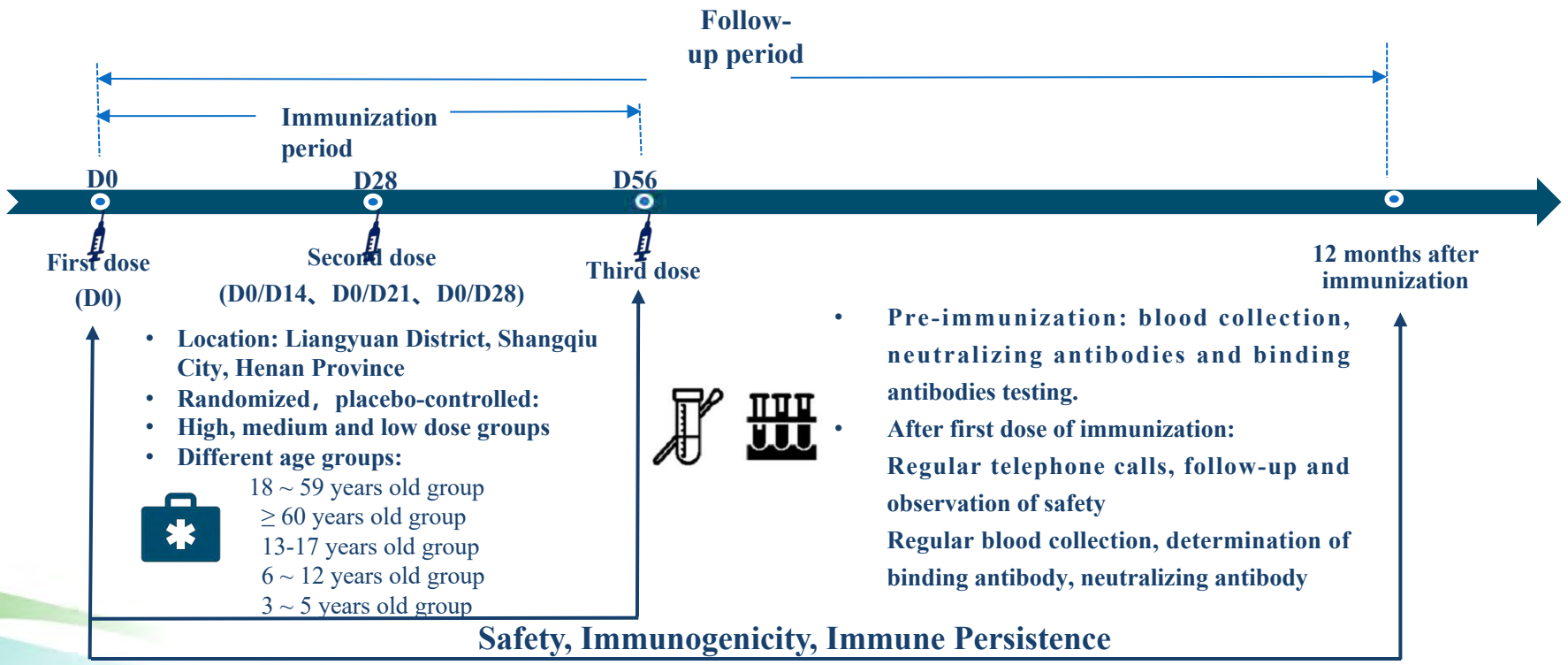
Wang, Hui, et al. *Development of an Inactivated Vaccine Candidate, BBIBP ...* www.cell.com/cell/pdf/S0092-8674(20)30695-4.pdf.

Clinical Studies

- Phase I and II Clinical Studies
- Phase III Clinical Studies

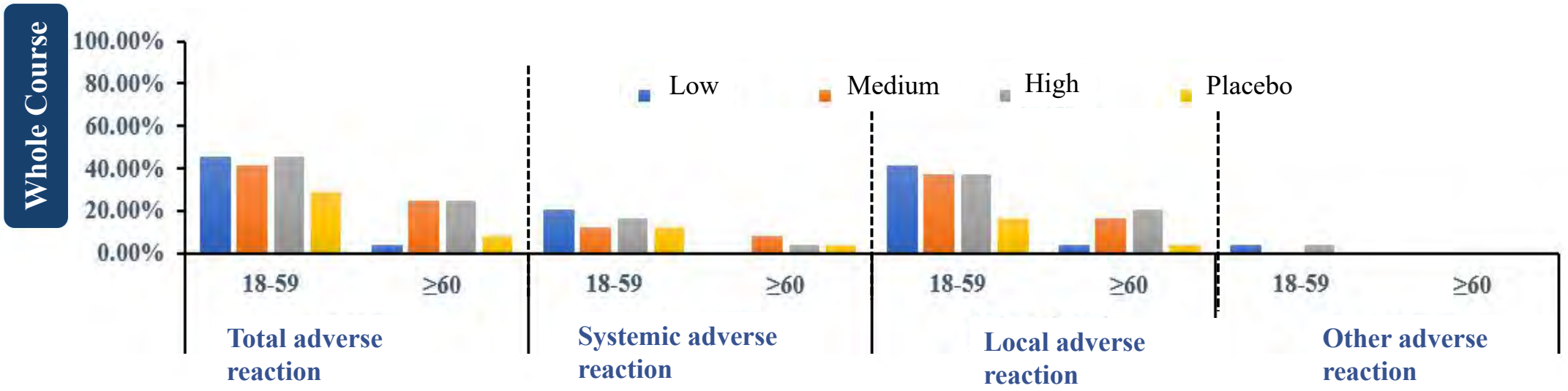
Phase I and Phase II Clinical Study Protocol

- **Study Objectives**
  Aimed to assess the safety and immunogenicity of an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidate
- **Phase I/II Study**
  Age Group: 3~5 years old, 6~12 years old, 13~17 years old, 18~59 years old, ≥ 60 years old
  Dosage: High, Medium and Low doses
  Immunization Schedules: D0 – D28 – D56
- **Phase II Study(middle doses)**
  Immunization Schedules: D0 – D28 – D56, D0 – D21 – D42, D0 – D14, D0 – D28, D0(high doses)



Phase I Clinical-Safety Results

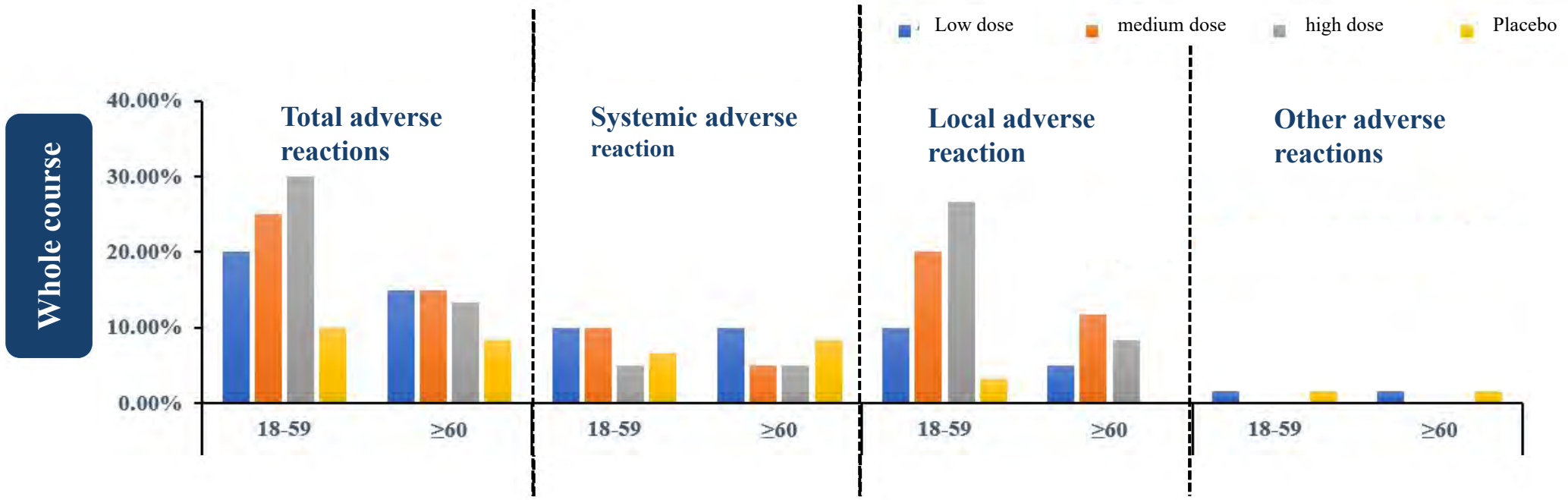
Incidence of adverse reactions after whole course of vaccination



- Within 0-30 days after the whole course vaccination, the total adverse reaction rates of the low/medium/high/placebo groups in the 18-59 year-old group were 45.83%, 41.67%, 45.83% and 29.17%, respectively.
- The total incidence of adverse reactions in low/medium/high/placebo group was 4.17%, 25%, 25% and 8.33% respectively in the group ≥ 60 years old.
- The incidence of total adverse reactions in the group ≥ 60 years old was lower than that in the group 18-59 years old.

Phase II Clinical - Safety Results

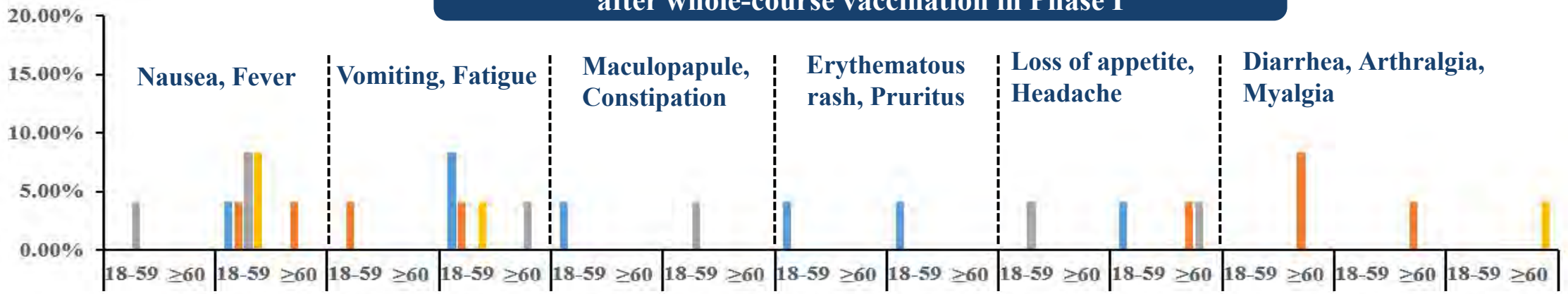
Incidence of adverse reactions 28 days after whole course vaccination



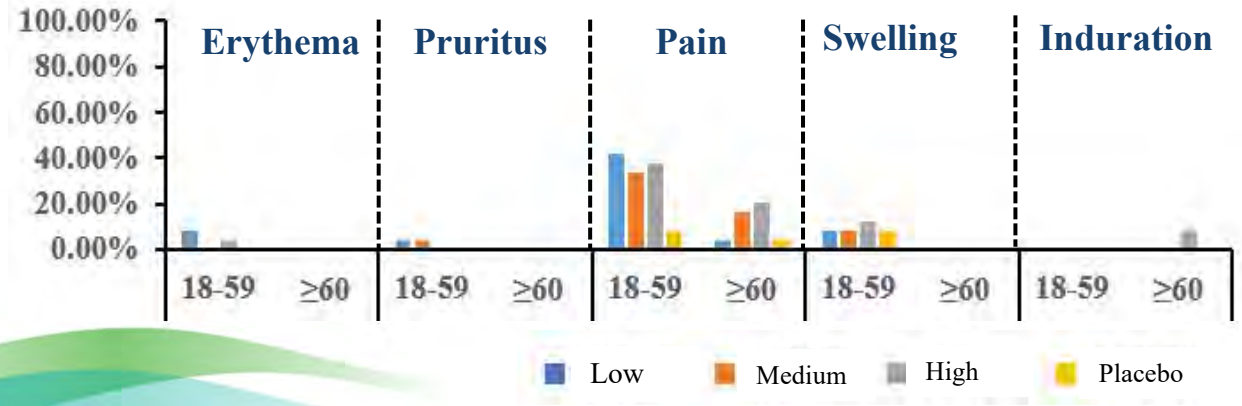
- **Within 0-30 days after the whole course vaccination, the total incidence of adverse reactions in the low/medium/high/placebo group of the 18-59 year-old group was 20%, 25%, 30% and 10%, respectively.**
- **The total incidence of adverse reactions in low/medium/high/placebo group was 15%, 15%, 13.33% and 8.33% respectively in group ≥ 60 years old.**
- **The incidence of total adverse reactions in the group ≥ 60 years old was lower than that in the group 18-59 years old.**

Phase I Clinical - Safety Results

Incidence of systemic adverse reactions by symptoms in 30 days after whole-course vaccination in Phase I



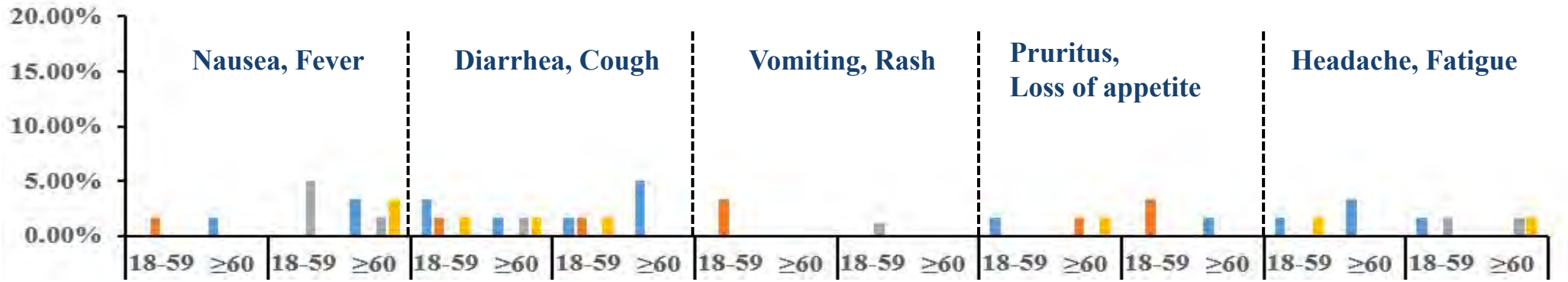
Incidence of local adverse reactions by symptoms in 30 days after whole-course vaccination in Phase I



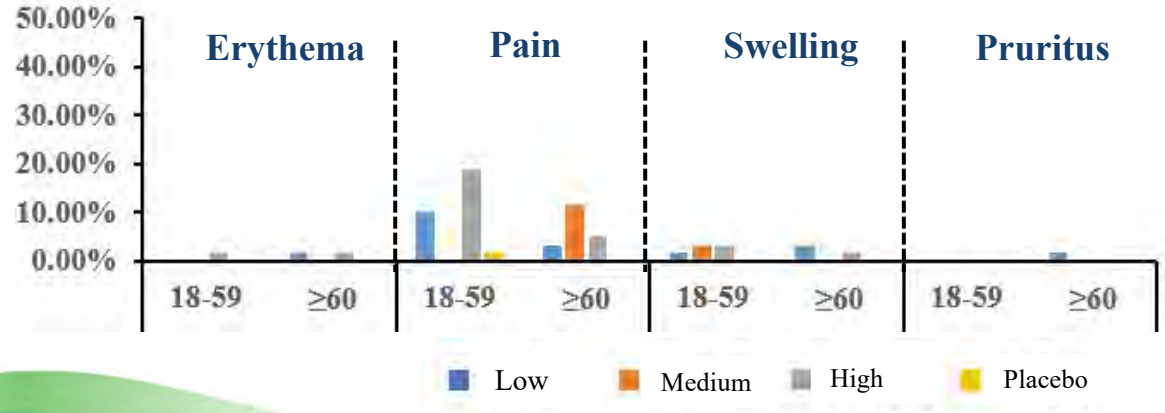
- **The incidence of systemic adverse reactions was low, mainly fever, with 4.17%, 4.17%, 8.33% and 8.33% in the low/medium/high dose group and placebo group respectively in the population aged 18-59 years old.**
- **The local adverse reactions were mainly pain, and the low/medium/high dose group and placebo group were 41.67%, 33.33%, 37.5% and 8.33% respectively.**

Phase II Clinical - Safety Results

Incidence of systemic adverse reactions by symptoms in 30 days after whole-course inoculation in Phase II



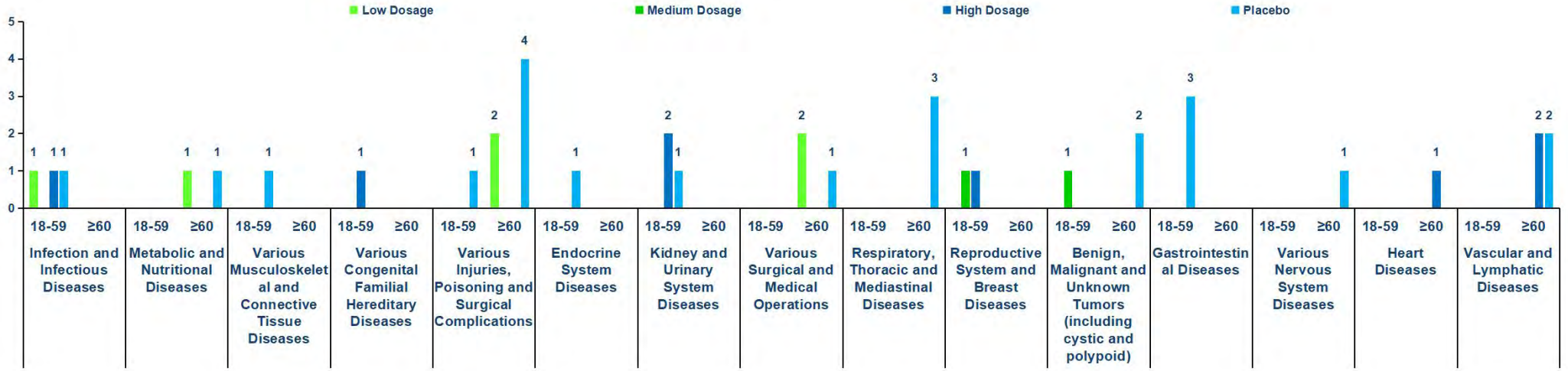
Incidence of local adverse reactions by symptoms in 30 days after whole-course inoculation in Phase II



- **The incidence of systemic adverse reactions is relatively low, mainly diarrhea and fever. The low/medium/high dose fever rates were 0%, 0% and 5% respectively in the 18-59 year-old population, and 3.33%, 0%, 1.67% and 3.33% respectively in the low/medium/high dose group and placebo group in the population aged ≥ 60 years old.**
- **Local adverse reactions were mainly pain, with 10.00%, 0%, 18.75% and 1.67% in low/medium/high dose group and placebo group respectively for 18-59 years old. The low/medium/high dose groups were 3.33%, 11.67% and 5.00% respectively in the population aged ≥ 60 years old.**

Phase I/II Clinical - SAE Results

SAE Incidence of Phase I/II Clinical Trial

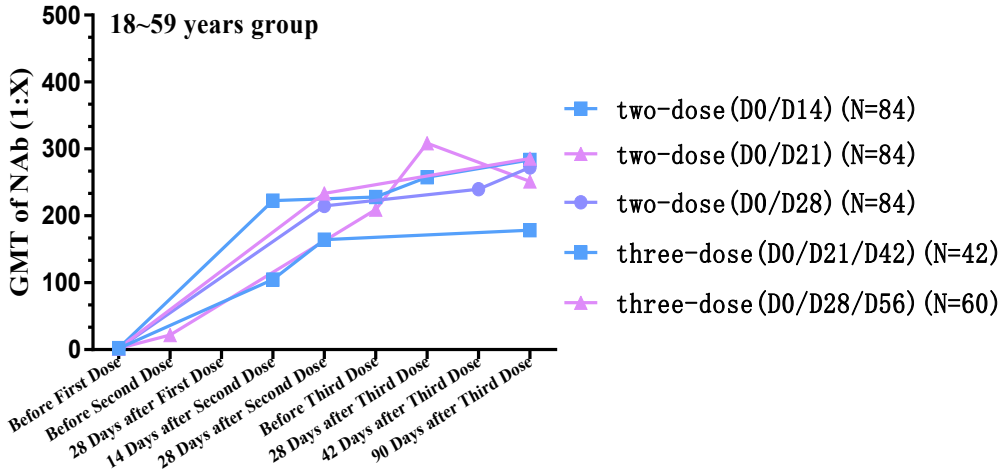


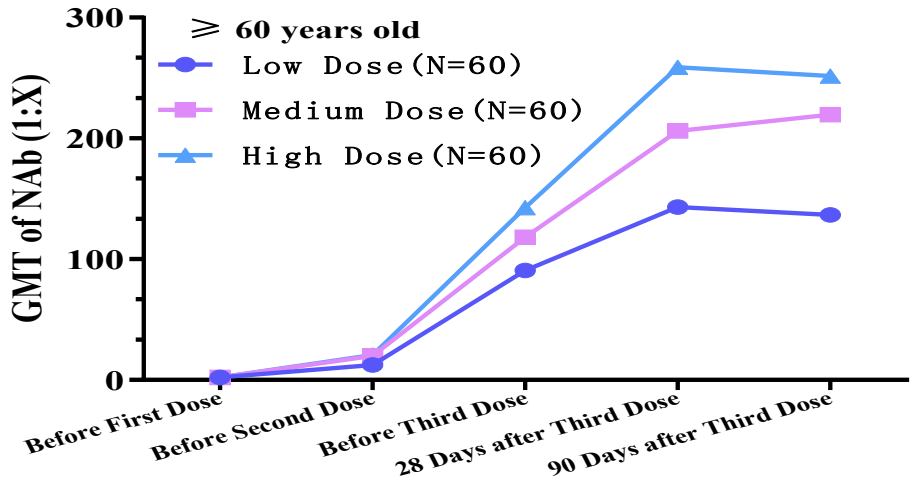
There were 13 subjects developed 38 SAEs in total.

They were all unrelated to vaccination.

Phase II Clinical - Immunogenicity Results

Results of Neutralizing Antibody after Full Course Immunization in Phase II





- The level of neutralizing antibody after two or three doses of immunization is significantly superior than that after one dose of immunization.
- In the two-dose immunization schedule, the neutralizing antibody level at D0/D21 and D0/D28 schedule are significantly better than that at D0/D14.

- After vaccination, population aged 60 and above can generate immune response.
- The antibody level in the high/medium dose groups were higher than that in the low dose group.

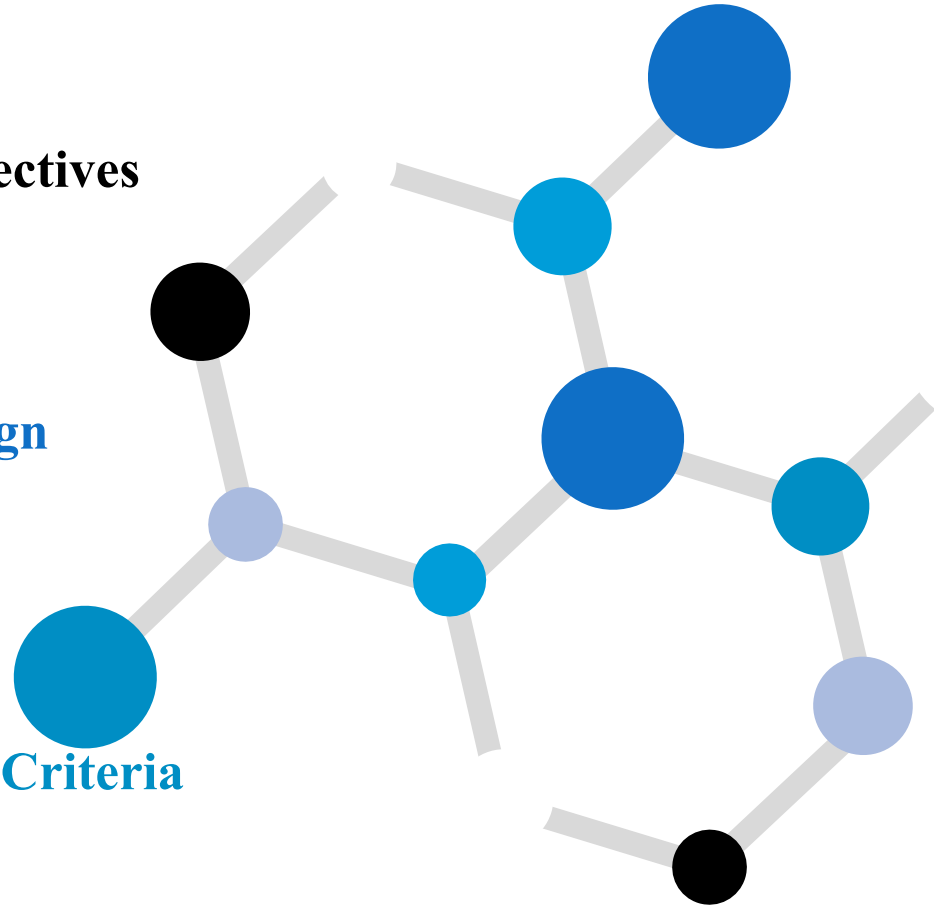
GMT of neutralizing antibody maintained at high level.
No significant reduction was observed until D90 after the last dose.

Phase III Clinical Study

Study Objectives

Study Design

Diagnostic Criteria



Efficacy

Safety

Immunogenicity

Study Objectives / Endpoints

Primary Objective

- Vaccine efficacy against COVID-19 among healthy population aged 18 years old and above

Secondary Objectives

- Vaccine efficacy against severe and death cases accompanied by COVID-19
- Immunogenicity
- Safety

Exploratory Objectives

- Protective efficacy of neutralizing antibody against COVID-19 (Immune surrogate Endpoint)
- Occurrence of ADE/VED after vaccination

Primary Endpoint

- Incidence of COVID-19 starting on day 15 after two doses of vaccination in healthy population aged 18 years and above.

Secondary Endpoint

- Severe and Death cases of COVID-19 starting on day 15 after 2nd dose of vaccination.
- Anti-SARS-CoV-2 neutralizing antibodies 4-fold rise, GMT
- Adverse events collected within dav 0~7．8～21/28davs

Exploratory Efficacy Endpoint

- The vaccine efficacy of neutralizing antibodies of SARS-CoV-2 against COVID-19.
- The incidence of ADE / VED following vaccination of SARS-CoV-2 inactivated vaccine.

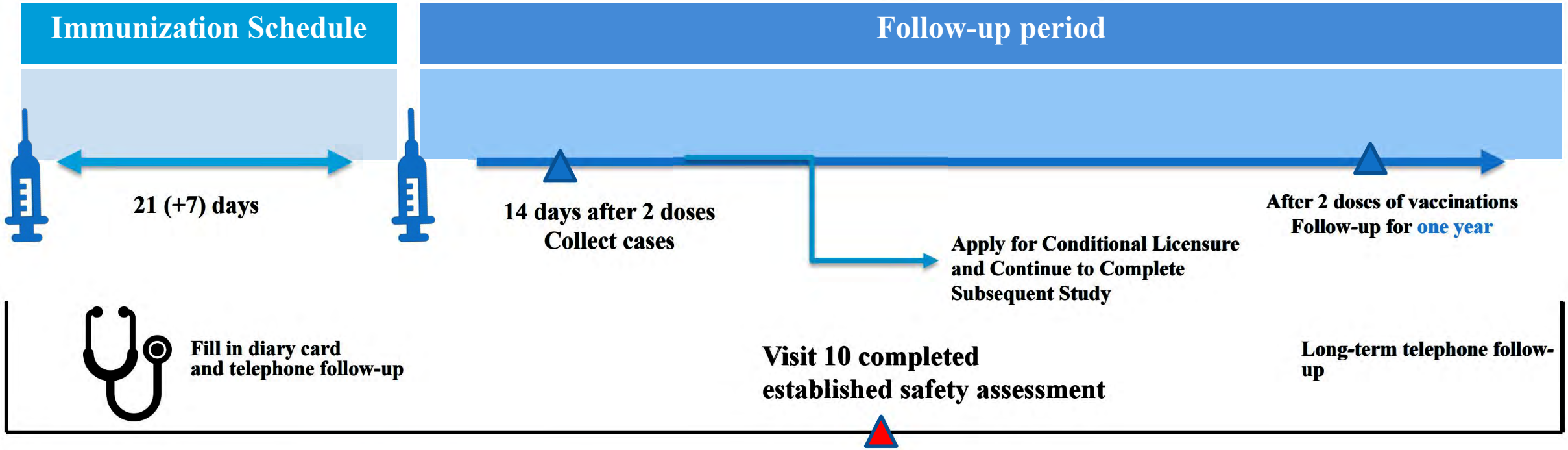
Study Design

- **Overall Design:** International Multi-center, Randomized, Double Blinded, Placebo Controlled Phase III Clinical Trial.
- **Protocol No.:** CNBG2020003SQ.
- **Investigational Vaccine:**

  Name: COVID-19 Vaccine (Vero Cell), Inactivated

  Manufacturer: Beijing Institute of Biological Products Co., Ltd., Wuhan Institute of Biological Products Co., Ltd., Wuhan Institute of Virus, Chinese Academy of Sciences.
- **Study Grouping:** The total sample size of approx 45000 subjects were randomly assigned to vaccine group 1, vaccine group 2 and placebo groups according to the ratio of 1: 1: 1.
- **Immunization Schedule:** According to the 0, 21 (+7) day immunization schedule, 2 doses of investigational vaccines or placebo are inoculated on the deltoid muscle of the upper arm. According to the results of immune persistence in Phase I/II clinical trials, the third dose (booster dose) will be vaccinated at an appropriate time.

Vaccination and Visit Procedure



Day 0
- ✓ First dose vaccination
- ✓ Blood collection before immunization

0-21 (+7) days
- ✓ Collect and evaluate the safety events after each dose of vaccine;
- ✓ Second dose vaccination

14 days after 2 doses of immunization
- ✓ Blood collection

28 days after 2 doses of immunization
- ✓ Blood collection

3 months, 6 months, 9 months and 12 months after 2 doses of immunization
- ✓ Blood collection

Diagnostic Criteria

Suspected cases

- Have any of the epidemiological history, and have two or more A symptoms, or have one or more B symptoms;
- If there is no clear epidemiological history, they should have two or more A symptoms or one or more B symptoms and detectable SARS-CoV-2 specific IgM; or have two or more A symptoms and One or more B symptoms; or with imaging features of COVID-19

Clinical symptoms

- Symptoms A (presence for at least 2 days, ≥48h): fever (axillary temperature ≥37.5℃); chills; sore throat; fatigue; nasal congestion or runny nose; body pain, muscle pain; headache; nausea or vomiting; diarrhea.
- Symptoms B: Cough (presence for at least 2 days, ≥48h); new taste or smell disorders(presence for at least 2 days, ≥48h); shortness of breath or difficulty breathing;

Confirmed cases

- On the basis of the determination of the suspected case, the COVID-19 PCR detection result is positive.

Clinical Classification

Mild

- The clinical symptoms were mild, and there was no sign of pneumonia on imaging.

Moderate

- Showing fever and respiratory symptoms with radiological findings of pneumonia.

Severe

- Respiratory distress (RR≥30 breaths/min);
- Oxygen saturation≤93% at rest;
- Arterial partial pressure of oxygen (PaO2)/ fraction of inspired oxygen (FiO2)≦300mmHg (1mmHg=0.133kPa);
- The clinical symptoms progressively worsened, and the chest imaging showed >50% obvious lesion progression within 24-48 hours.

Critical

- Respiratory failure and requiring mechanical ventilation;
- Shock;
- With other organ failure that requires ICU care;
- Death

Phase III Clinical Sites

CNBG's COVID-19 Vaccine (Vero Cell), Inactivated, has been carrying out large-scale phase III efficacy clinical studies in the United Arab Emirates (UAE) and four other countries. As of December 31, 2020, nearly 45000 people had been enrolled.

Clinical Center	Recruitment and Vaccination		
	Recruitment	First Dose Subjects	Second Dose Subjects
Abu Dhabi, UAE	27,391	27,362	26,537
Sharjah, UAE	5,265	5,265	5,174
Bahrain	7,755	7,755	7,512
Egypt	3,000	2,991	2,828
Jordan	480	478	450

Demographic Data and Baseline Characteristics

Characteristic	Statistics	HB02	Placebo
Age, n(%)	18 - 59 years	14338 (97.99)	14313 (98.00)
	≥ 60 years	294 (2.01)	292 (2.00)
Gender, n(%)	Female	2293 (15.72)	2247 (15.42)
	Male	12294 (84.28)	12327 (84.58)
Populations, n(%)	Asian	12619 (86.23)	12702 (86.96)
	Non-Asian	2015 (13.77)	1904 (13.04)
Country, n(%)	Chinese	1837 (12.55)	1866 (12.78)
	Non-Chinese	12740 (87.22)	12797 (87.45)

The median follow-up time was 112 days.

Second Interim Analysis

The second interim analysis is based on the data as of December 31, 2020.

According to the judgment of EAC and agreement among regulatory authorities, the total number of cases is 116, of which 95 were in placebo group, and 21 were in HB02 group. The number of cases required for the second interim analysis is 100.

DSMB 针对评价新型冠状病毒灭活疫苗（Vero 细胞）在 18 岁及以上健康人群中接种后保护效力、安全性和免疫原性的国际多中心、随机、双盲、安慰剂平行对照III期临床试验的建议书

会议日期：2020 年 11 月 12 日

会议形式：[illegible]

参会人员：夏结来、[illegible]

本次会议审核的评价新型冠状病毒灭活疫苗（Vero 细胞）在 18 岁及以上健康人群中接种后保护效力、安全性和免疫原性的国际多中心、随机、双盲、安慰剂平行对照III期临床试验的截止 2020 年 10 月 30 日的保护效力数据和 2020 年 10 月 31 日的安全性数据。本次数据分析是基于新型冠状病毒灭活疫苗（Vero 细胞）III期临床试验数据库V3.0（20201111 1723），纳入病例是基于 2020 年 11 月 11 日由终点事件判定委员会判定的病例。

DSMB 给出了如下建议（在下列建议中适用的打钩）：

[√] 研究达到试验方案预设的有效性标准：

[ ]武汉生物制品研究所有限责任公司

[ ]北京生物制品研究所有限责任公司

[√]武汉生物制品研究所有限责任公司和北京生物制品研究所有限责任公司

[ ] 按照现有方案，继续进行下一阶段临床研究；

[ ] 按照现有方案，继续进行研究，但提前召开下次会议，建议日期为：____年____月____日；

[ ] 按照现有方案，继续进行研究，但增加一次临时会议；

描述临时会议的时间及内容。

[ ] 继续进行研究，但需对方案进行修改；

描述修改主要的内容。

[ ] 暂停入组，直到如下问题得到解决；

描述需要解决的问题。

[ ] 中止研究，原因为：

[√] 其他对申办者的意见和建议：

(1) 继续对入组受试者进行安全性和有效性观察。

(2) 可以考虑停止受试者招募。

DSMB 主席/成员签字： 日期 2020.11.12

1

Primary Efficacy Results (mFAS-1)

Vaccine efficacy against COVID-19 cases after 14 days post full course of immunization-based on person-year incidence

	Placebo	HB02
Total Number of Subjects	13765	13765
Number of Cases	95	21
Person-Year Incidence (95%CI)	4.40%(3.60%, 5.38%)	0.96% (0.63%, 1.48%)

HB02 vs placebo (≥18 years old)

- **The vaccine efficacy was 78.07%**
- **The two-sided 95% CI was (64.82%, 86.33%)**
- **Two-sided 95% CI lower limit is greater than 30%.**

Primary Efficacy Results (mFAS-1 Sensitivity Analysis)

Vaccine efficacy against COVID-19 cases after 14 days post full course of immunization-based on person-year incidence

	Placebo	HB02
Total Number of Subjects	13765	13765
Number of Cases	94	20
Person-Year Incidence (95%CI)	4.35%(3.55%, 5.32%)	0.92% (0.59%, 1.42%)

HB02 vs placebo (≥18 years old)

- The vaccine efficacy was 78.89%
- The two-sided 95% CI was (65.79%, 86.97%)
- Two-sided 95% CI lower limit is greater than 30%.

Efficacy against Severe Covid-19

Vaccine efficacy against COVID-19 severe cases after 14 days post full course of immunization-based on person-year incidence

	Placebo	HB02
Total Number of Subjects	13765	13765
Number of Cases	2	0
Person-Year Incidence (95%CI)	0.09%(0.01, 0.33)	0.00% (0.00, 0.17)

HB02 vs placebo (≥18 years old)

- The vaccine efficacy was 100.00%
- The two-sided 95% CI was (-430.26, 100.00)

Primary Efficacy Results – Subgroup Analysis (mFAS-1)

Subgroup		Placebo (N=13765)	HB02 (N=13765)	VE (%)	95%CI
Age	18-59	95	21	78.09	(64.85, 86.34)
	60 and above	0	0	NE	NE
Gender	Male	83	18	78.43	(64.09, 87.04)
	Female	12	3	75.54	(13.34, 93.1)
Ethnicity	Asian	89	18	79.76	(66.42, 84.81)
	Chinese	0	0	NE	NE
Baseline	IgG Positive	1	0	100	(-3395.15, 100)
	IgG Negative	83	16	80.79	(67.19, 88.75)

Primary Efficacy Results – Subgroup Analysis (mFAS-1)

Subgroup		Placebo	HB02	VE (%)	95%CI
BMI≥30	No. of participants	3080	3040	80.72	(56.67,91.42)
	No. of incident cases	36	7		
Asymptomatic Infection	No. of participants	13765	13765	50.39	(-2.30, 75.94)
	No. of incident cases	22	11		
Comorbidity	Hypertension	4 (367)	0 (374)	100	(-,100)
	Diabetes	6 (308)	2 (300)	63.71	(-79.79,92.68)
	CVDs	1 (67)	0 (73)	100	(-,100)

Number of COVID-19 Cases - between Randomization and 14 Days after 2nd Dose of Vaccination

	Surveillance Period	Non-Surveillance Period	Total
Placebo Group	95	43	138
HB02 Group	21	27	48

- The confirmed COVID-19 casas in placebo group were 138, which included 95 surveillance cases and 43 non-surveillance cases.
- The confirmed COVID-19 casas in HB02 group were 48, which included 21 surveillance cases and 27 non-surveillance cases.

Primary Efficacy Results (mFAS-1 Sensitivity Analysis)

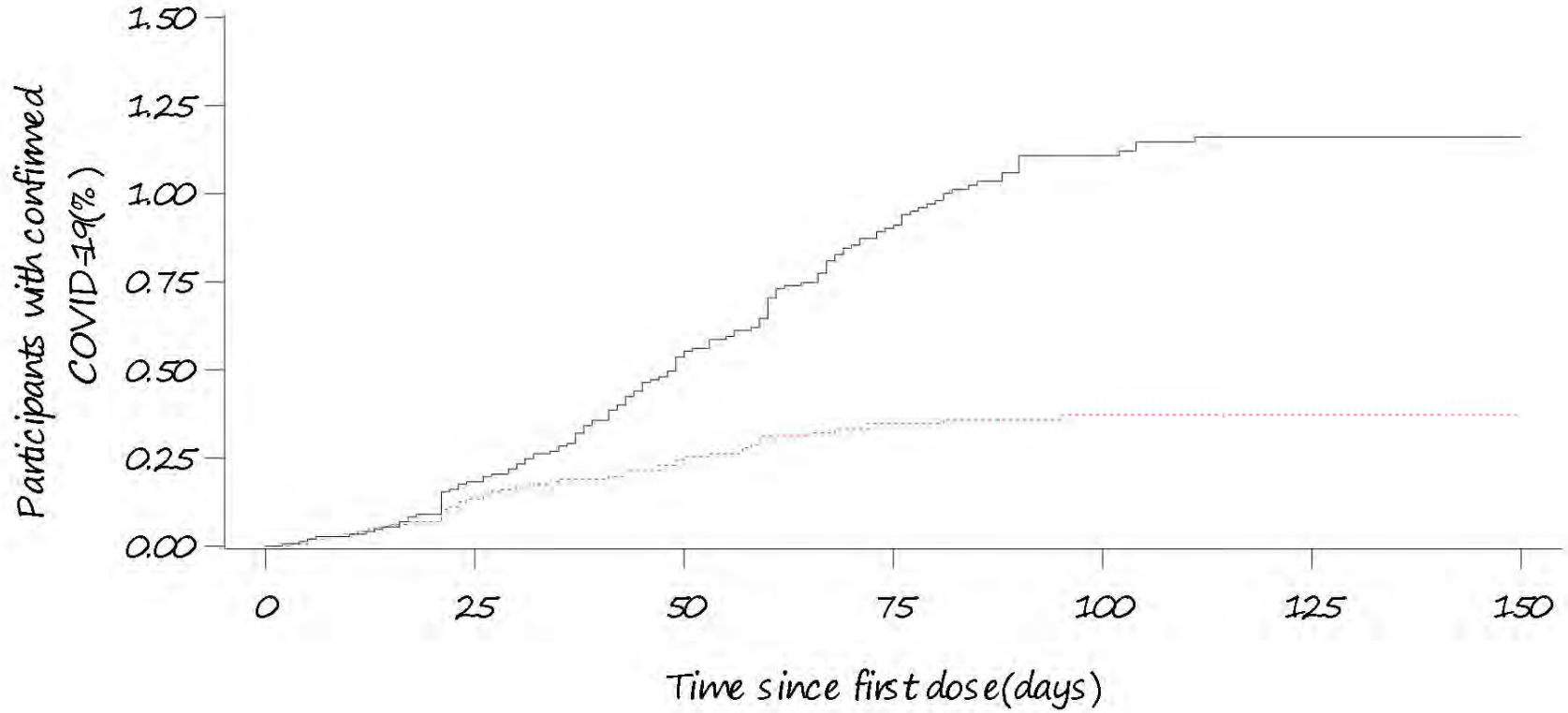
Vaccine efficacy against COVID-19 cases after 1st dose-based on person-year incidence

	Placebo	HB02
Total Number of Subjects	14574	14587
Number of Cases	138	48
Person-Year Incidence (95%CI)	3.9%(3.3,4.61)	1.35%(1.02,1.79)

HB02 vs placebo (≥18 years old)

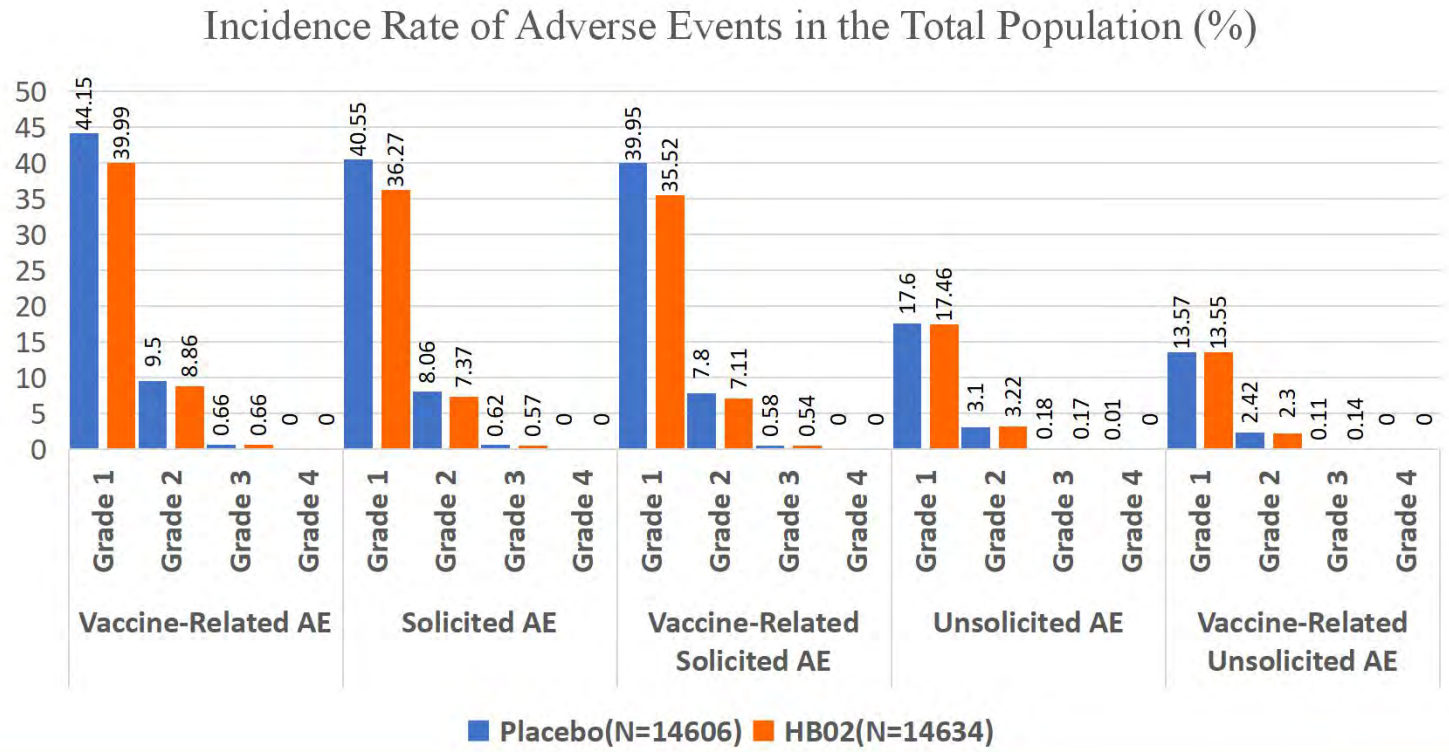
- **The vaccine efficacy was 65.45%**
- **The two-sided 95% CI was (52.02,75.12)**

Kaplan-Meier Estimates - Time to First Occurrence of COVID-19 since the First Dose of Vaccination



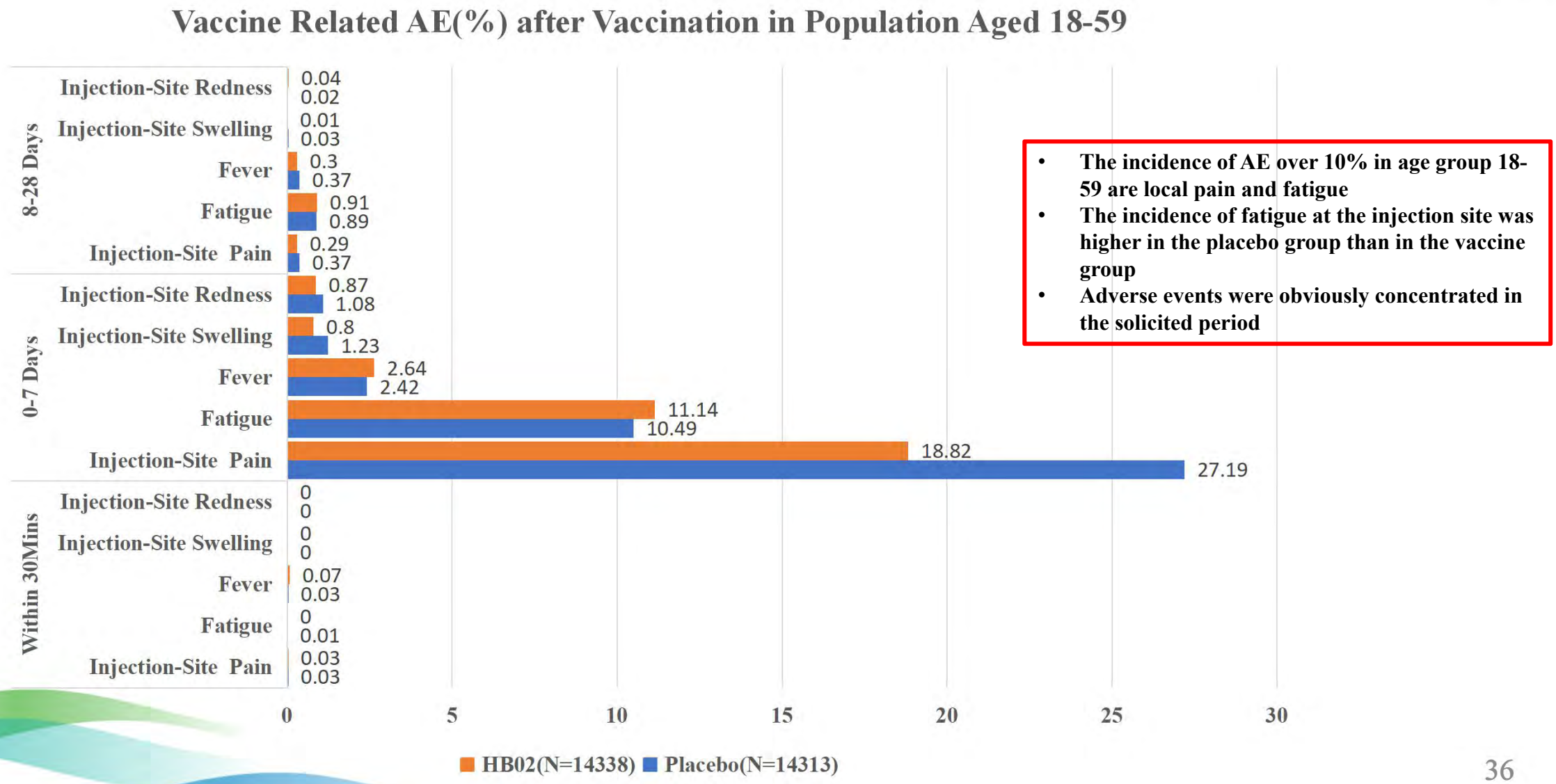
HB02 n	14587	13840	11810	8153	653	0
Placebo n	14574	13795	11704	8060	665	1

Safety - Total Adverse Event Incidence



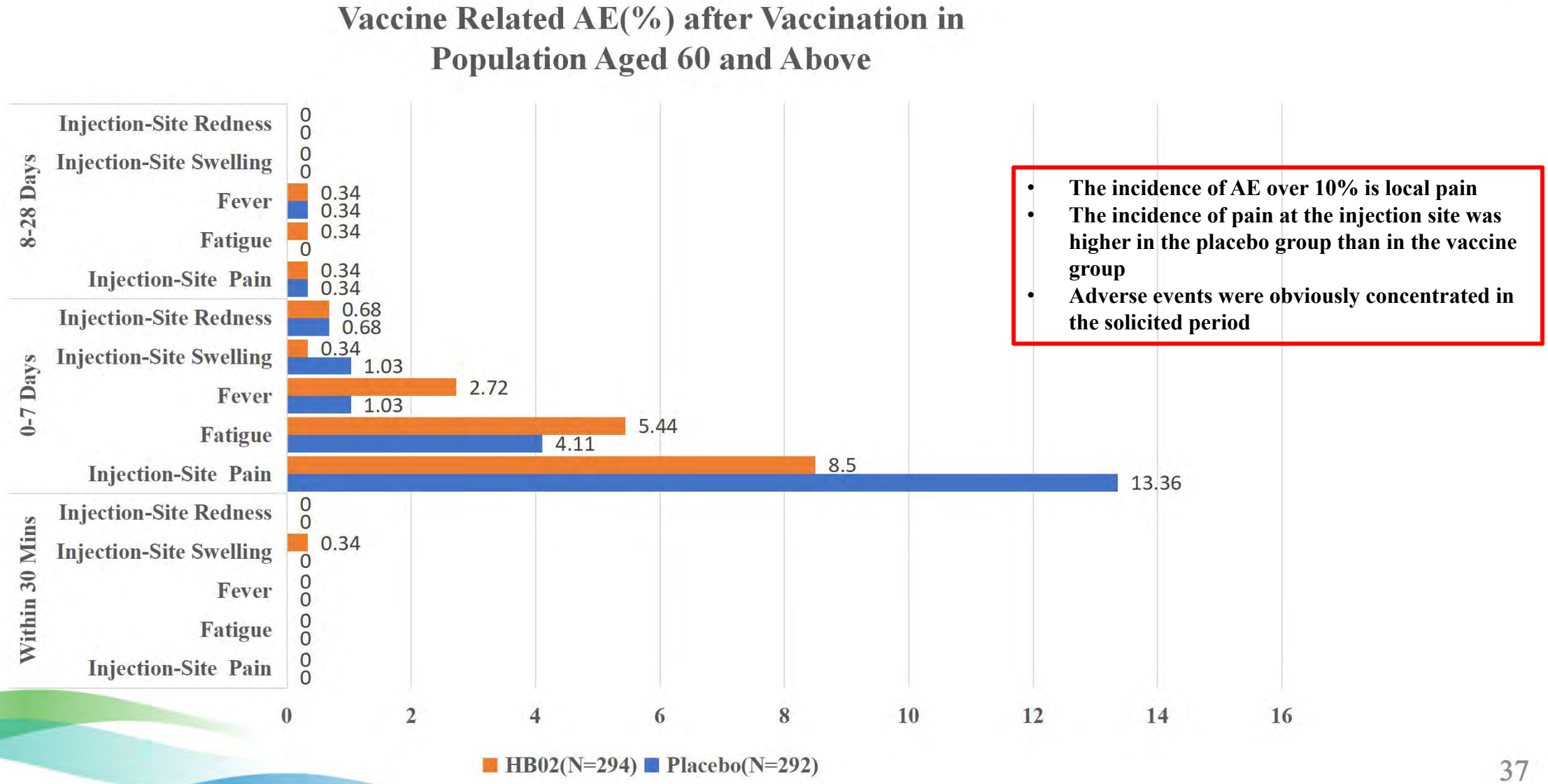
- **The total cases of adverse events (times) in placebo group and HB02 vaccine group were 7,159 (17,547) and 6,570 (16,057) respectively, with the incidence rates of 49.01% and 44.90% respectively.**
- **Majority of the adverse reactions were grade 1.**
- **The incidence of Grade 1 adverse events in placebo group was higher than that in vaccine group, and the difference between groups was statistically significant. There was no significant difference between the two groups in other classifications.**

Vaccine Related AE in Population Aged 18-59 - Categorized by Time



- The incidence of AE over 10% in age group 18-59 are local pain and fatigue
- The incidence of fatigue at the injection site was higher in the placebo group than in the vaccine group
- Adverse events were obviously concentrated in the solicited period

Vaccine Related AE in Population Aged 60 and Above - Categorized by Time



- The incidence of AE over 10% is local pain
- The incidence of pain at the injection site was higher in the placebo group than in the vaccine group
- Adverse events were obviously concentrated in the solicited period

Occurrence of Allergic Reaction after vaccination

	Placebo (N=14297)				HB02 (N=14310)				
	All AE		Related AE		All AE		Related AE		
	Number of Cases	Incidence (%)	Number of Cases	Incidence (%)	Number of Cases	Incidence (%)	Number of Cases	Incidence (%)	P-Value
Acute Allergic Reaction	1	0.01	1	0.01	2	0.01	1	0.01	0.9096
Hypersensitivity Reaction	48	0.34	42	0.29	49	0.34	48	0.3	0.9847

The vaccine-related AE incidence of allergic reaction in Placebo group and HB02 group were both 0.01, and there was no significant difference between two groups.

SAE Incidence

Summary of Post-Vaccination SAEs (SS)

	Placebo (N=14606)			HB02 (N=14634)		
	Times	Cases	Incidence(%)	Times	Cases	Incidence(%)
Total SAEs	114	80	0.55	129	59	0.40
Related to Investigational Vaccine	0	0	0.00	6	2	0.01
Unrelated to Investigational Vaccine	114	80	0.55	123	57	0.39

SAE Incidence

Summary of SAEs after Vaccination among Different Ages and Different Populations (SS)

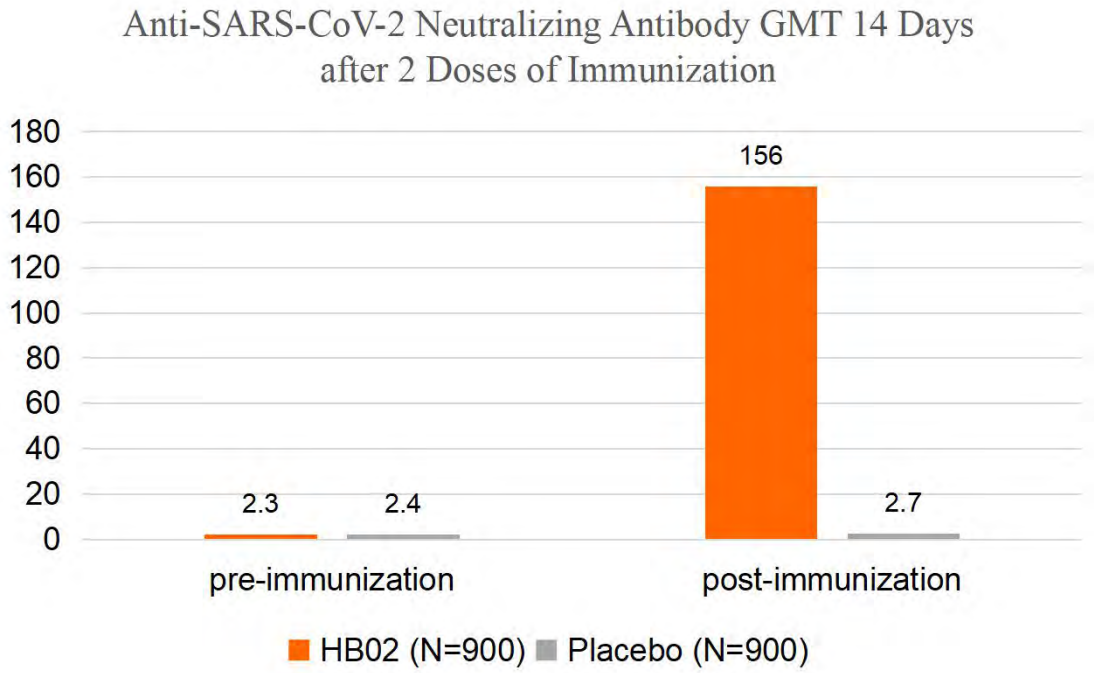
	Placebo (N=14606)			HB02 (N=14634)		
	Times	Cases	Incidence(%)	Times	Cases	Incidence (%)
18-59 Years Old	113	79	0.55	129	59	0.41
60 Years Old and above	1	1	0.34	0	0	0.00
Asian	103	72	0.57	113	52	0.41
Baseline PCR Positive	0	0	0.00	0	0	0.00
Chinese	3	3	0.16	0	0	0.00

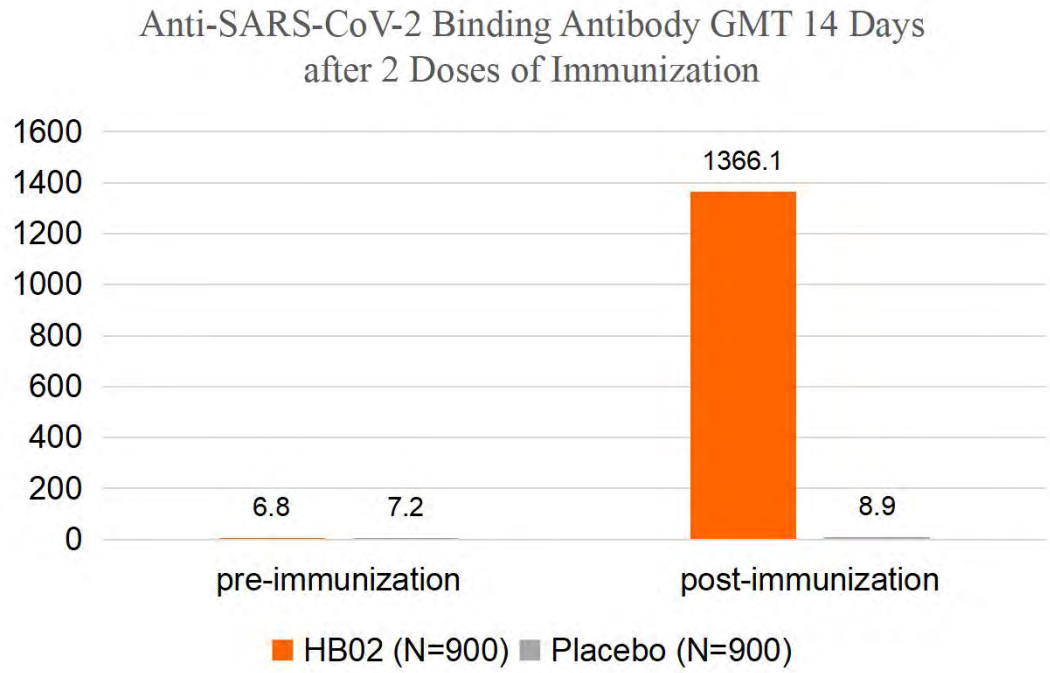
Pregnancy Event Incidence

Pregnancy Event Incidence（SS）

	Placebo (N=14631)	HB02 (N=14630)
Pregnancy Subject (%)	8 (0.05%)	5 (0.03%)
Pregnancy Times	8	5
Delivery(%)	0	0
Non-delivery(%)	8 (0.03%)	5 (0.03%)

Immunogenicity





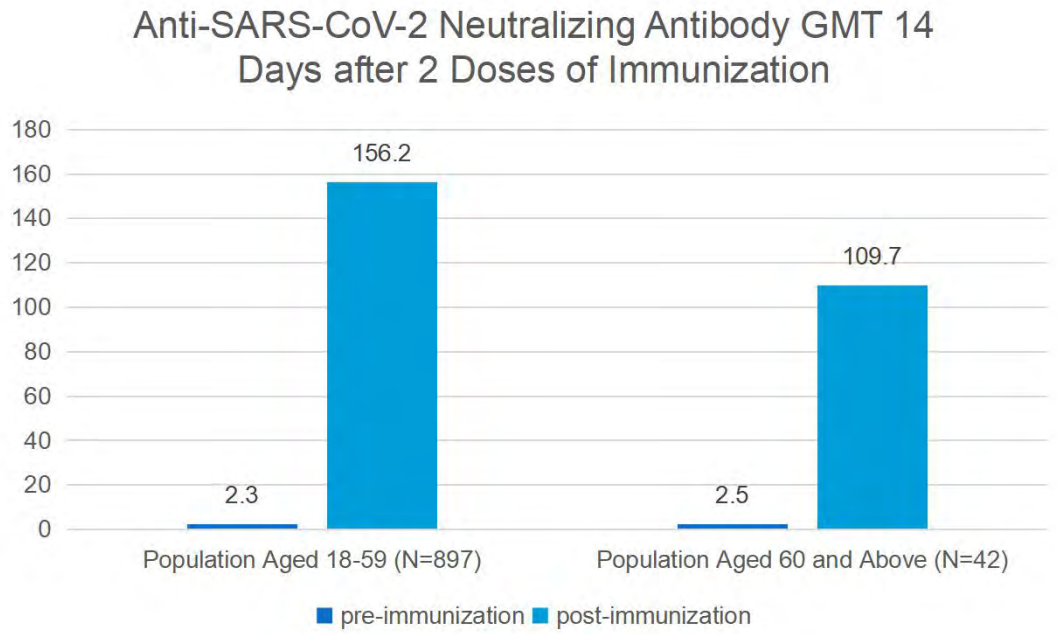
Neutralizing Antibody GMT:

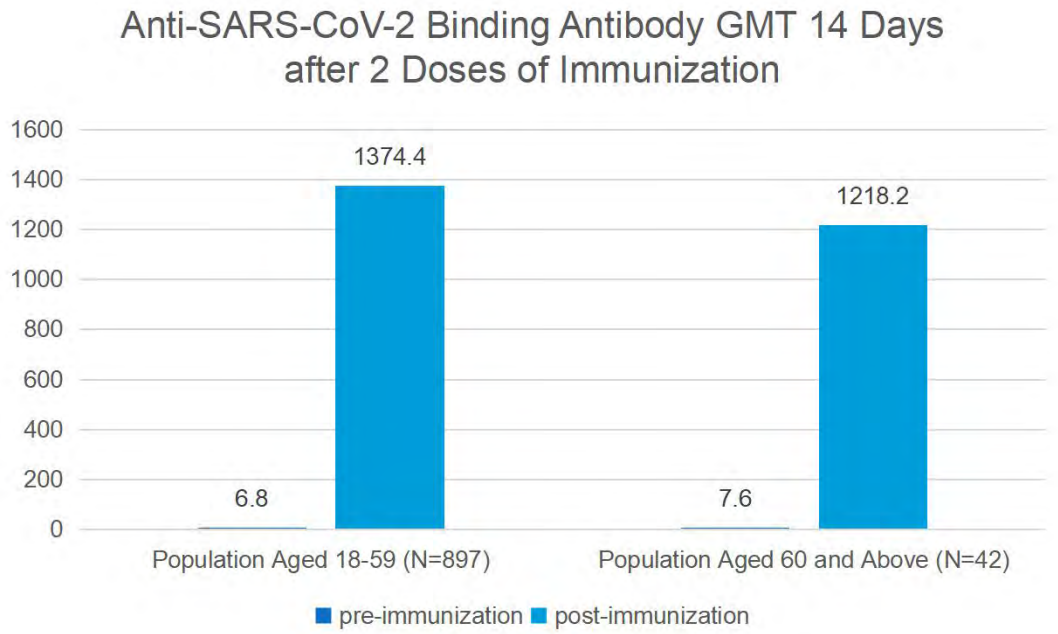
- 14 days after 2 doses, the anti-SARS-CoV-2 neutralizing antibody GMT in HB02 group is 156.
- Anti-SARS-CoV-2 neutralizing antibody have obvious increase.

Binding Antibody GMT:

- 14 days after 2 doses, the anti-SARS-CoV-2 binding antibody GMT in HB02 group is 1366.1.
- Anti-SARS-CoV-2 binding antibody have obvious increase.

Immunogenicity - Different Age Group





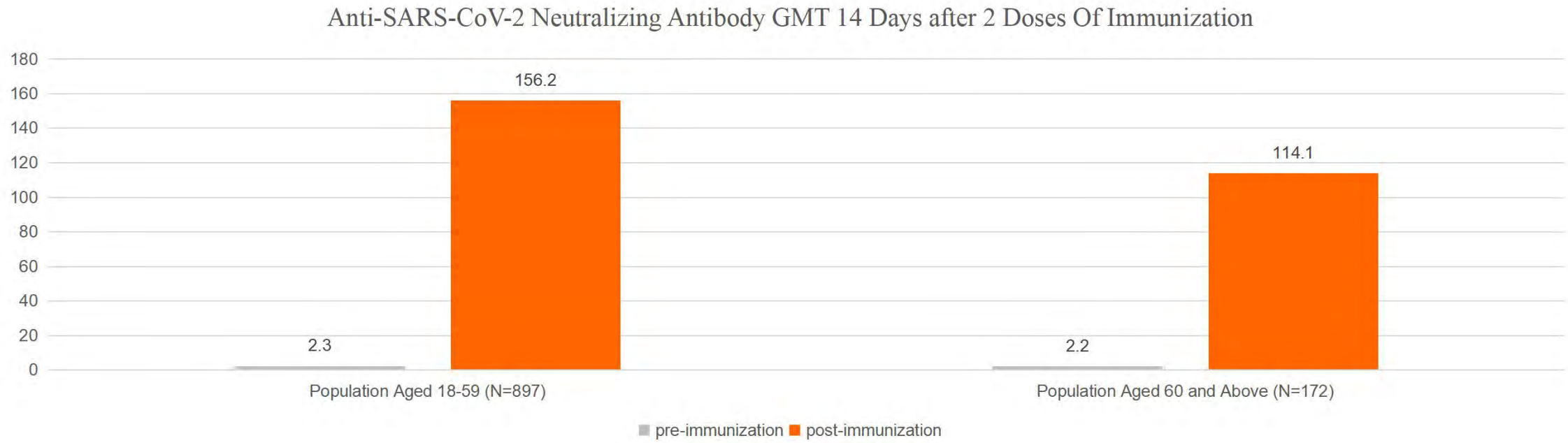
Neutralizing Antibody GMT:

- 14 days after 2 doses, the anti-SARS-CoV-2 neutralizing antibody GMT in HB02 group for population aged 18-59 and 60 and above are 156.2 and 109.7 respectively.
- Anti-SARS-CoV-2 neutralizing antibody for two different aged groups have obvious increase.

Binding Antibody GMT:

- 14 days after 2 doses, the anti-SARS-CoV-2 binding antibody GMT in HB02 group for population aged 18-59 and 60 and above are 1374.4 and 1218.2 respectively.
- Anti-SARS-CoV-2 binding antibody for two different aged groups have obvious increase.

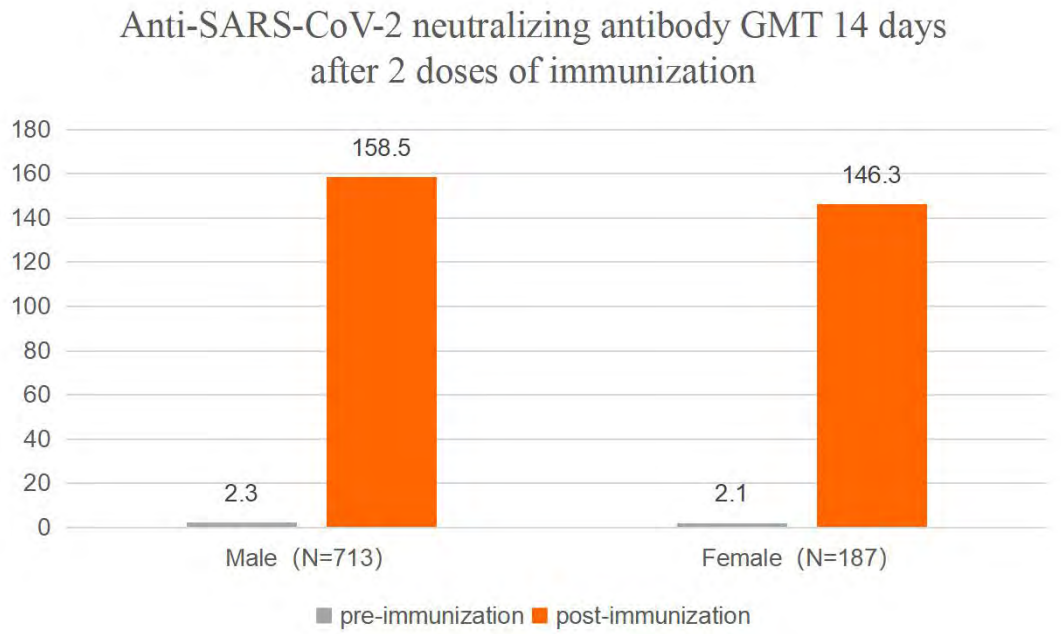
Immunogenicity - Phase III 18-59 VS Phase I/II/III 60 and above

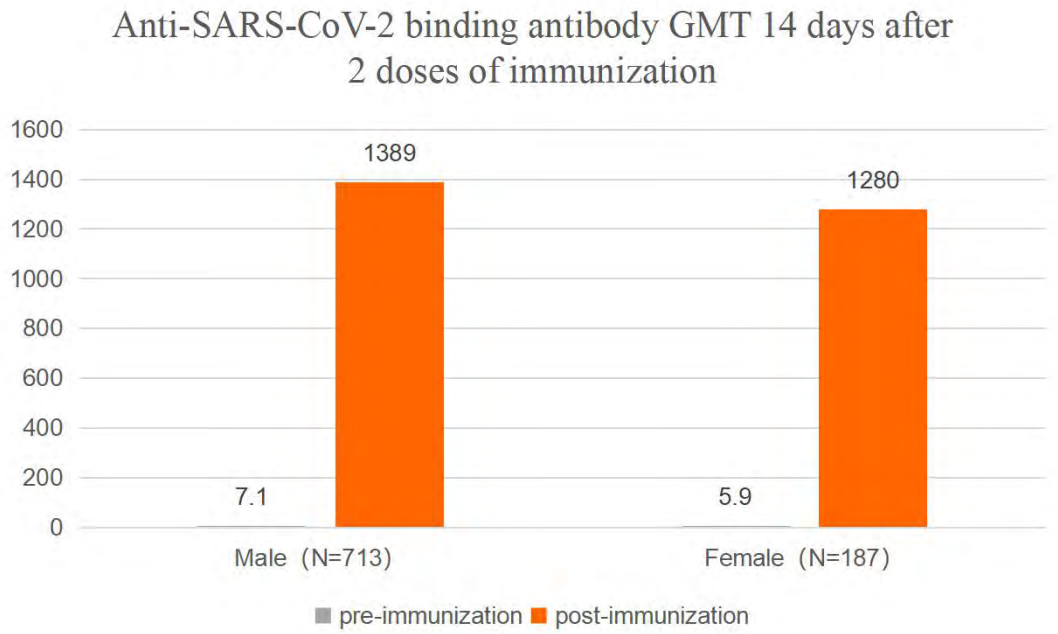


Neutralizing Antibody GMT:

- 14 days after 2 doses, anti-SARS-CoV-2 neutralizing antibody GMT in HB02 group for population aged 18-58 and 60 and above are 156.2 and 114.1 respectively.
- Anti-SARS-CoV-2 neutralizing antibody for two different aged groups have obvious increase.

Immunogenicity - Gender





Neutralizing Antibody GMT:

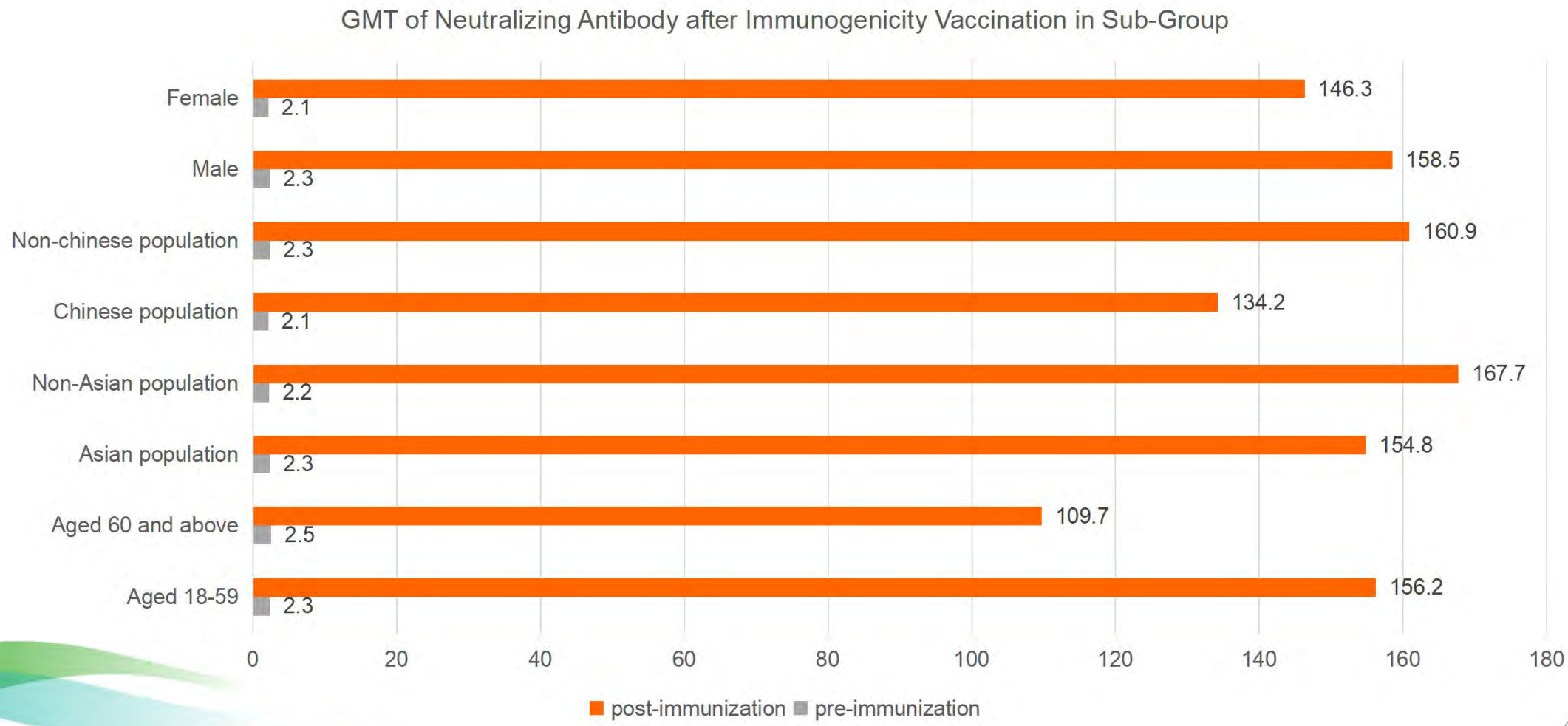
- 14 days after 2 doses, anti-SARS-CoV-2 neutralizing antibody GMT in HB02 group for male and female are 158.5 and 146.3 respectively.
- Anti-SARS-CoV-2 neutralizing antibody for different genders have obvious increase.

Binding Antibody GMT:

- 14 days after 2 doses, anti-SARS-CoV-2 binding antibody GMT in HB02 group for male and female are 1389 and 1280 respectively.
- Anti-SARS-CoV-2 binding antibody for different genders have obvious increase.

Immunogenicity - Subgroup

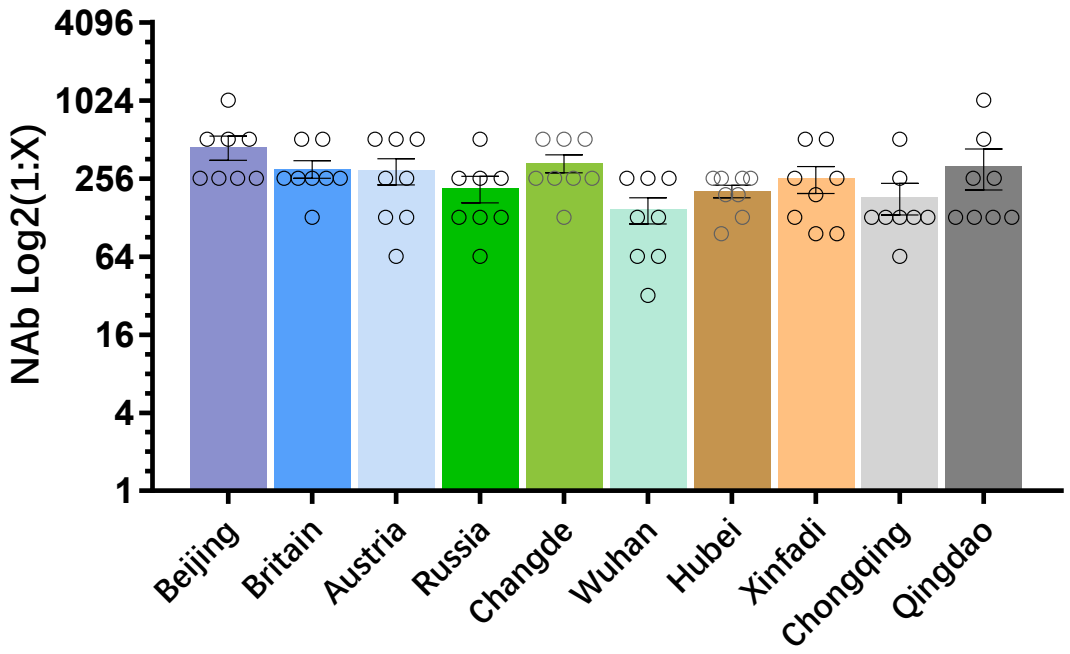
The GMT Level of Serum Neutralizing Antibody in Each Subset 14 Days after Immunization



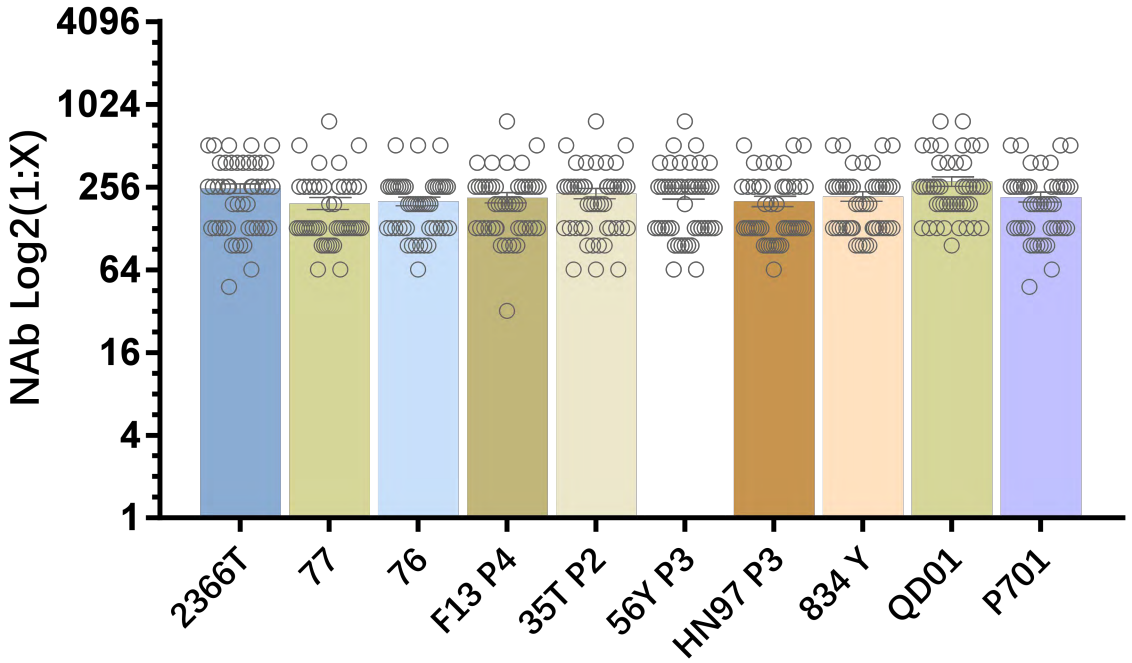
Phase I/II/III Clinical Cross-Neutralization Results

Cross-protection of Neutralizing Antibodies against Multiple Prevalent Strains

Results of Cross-Neutralizing (Phase 1/2)



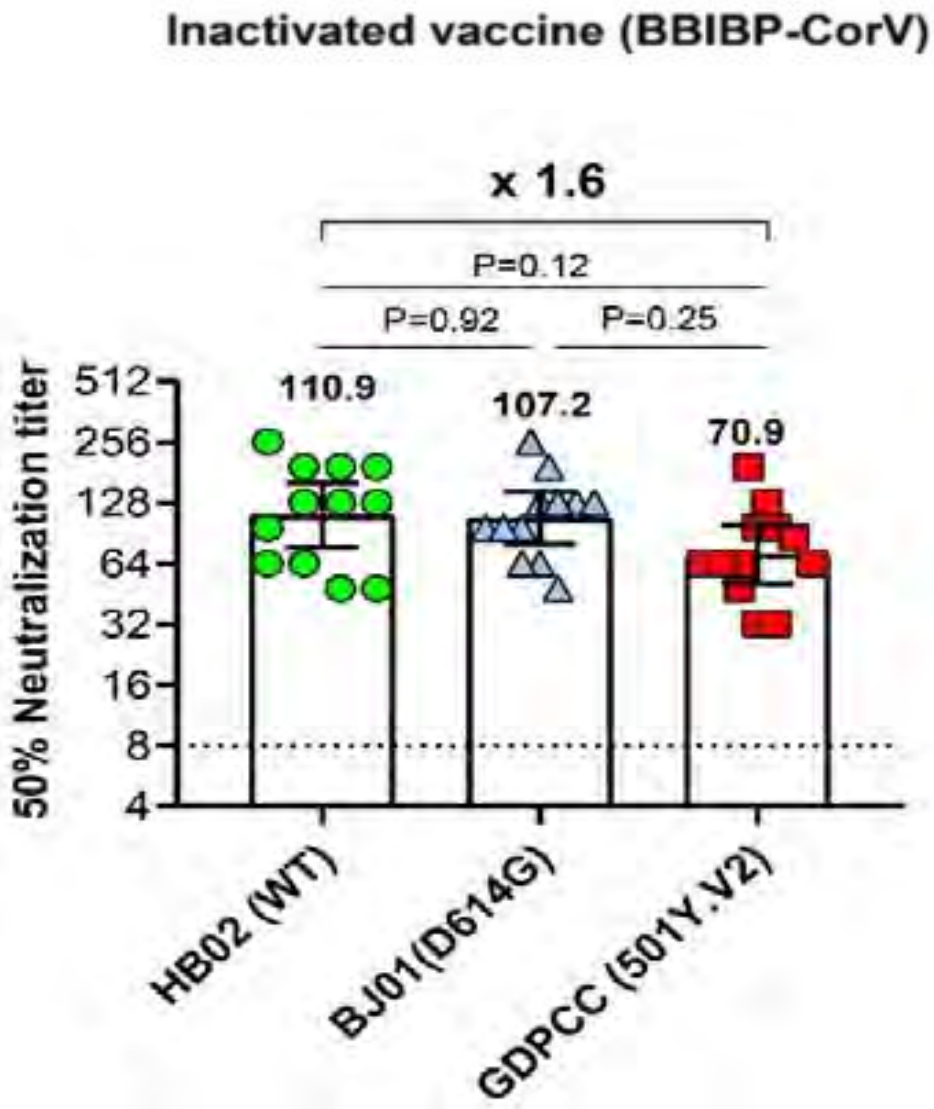
Results of Cross-Neutralizing (Phase 3)



Phase I-III clinical serum:

Has high cross neutralization activity against multiple prevalent SARS-CoV-2 strains, showing broad cross protection.

Cross-Neutralization against 501Y.V2



Summary of Phase III Second Interim Analysis

◆ **Vaccine Efficacy**

- The vaccine efficacy based on the person-year incidence rate of population aged 18 years old and above reached 78.89%, achieved the primary efficacy endpoint.
- The vaccine efficacy against severe cases of COVID-19 in population aged 18 years old and above is 100%, achieved the secondary efficacy endpoint.

◆ **Safety**

- Within 28 days after the second vaccination, placebo group and HB02 group had an AE incidence of 49.01% and 44.90%, respectively.
- Population aged 60 (29.25%) and above had lower AE incidence than population aged 18-59 (45.22%) after 2 doses of vaccination.
- Adverse event was mainly concentrated on grade 1 AE, and the grade 3 AE had an incidence of 0.77%. No grade 4 vaccine related AE.

◆ **Immunogenicity**

- After 14 days following 2 doses of immunization, the positive seroconversion rate (4 fold growth rate), GMT and GMI of anti-SARS-CoV-2 neutralizing antibody were 100%, 156.0 and 68.689 respectively, which were significantly higher than those of placebo group.

Summary of Phase III Second Interim Analysis

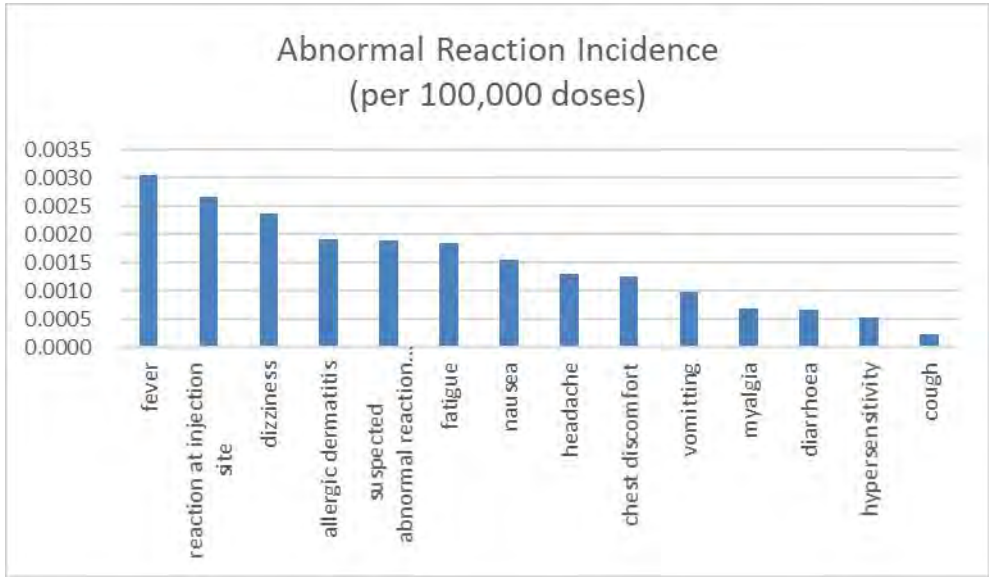
◆ **Cross-Neutralization Protection Effect of Subject Serum**

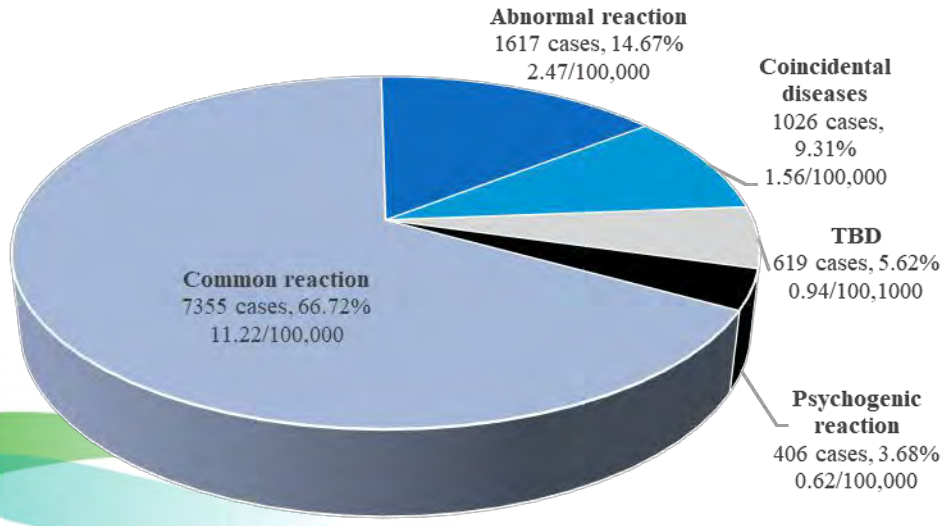
- The results of the true virus cross-neutralization test by blindly drawing serum samples from the subjects in this phase III clinical trial showed that, the serum of HB02 groups at 28 days after whole immunization had good cross-neutralization ability with 10 SARS-CoV-2 strains epidemic at domestic and abroad.
- The positive seroconversion rate of neutralizing antibody in HB02 groups can reach 100%, and there is no significant difference in antibody titers among these strains. The vaccines have extensive cross neutralization reactions to the current domestic and abroad epidemic or representative SARS-CoV-2 Wild Viruses.

Post-marketing activities

- **Post-marketing surveillance**
- **Post-marketing clinical studies**

The Adverse Reaction after launch





- As of 31 March 2021, AEFI reports from 65.58 million people vaccinated have been obtained;
- Common reactions: 7355 cases reported (11.22 /100,000)
- Local reactions: redness, swelling, and induration ; mainly mild
- Systemic reactions: fever, fatigue, headache, dizziness

- Abnormal (rare) reactions; 1617 reported (2.47 /100,000) were reported
- Most common reactions were allergic rash, other allergic reactions, and urticarial

- Male：37.4%；female：62.58%
- Age：majority are 18-59 years old，≥60 years:79 cases

The Adverse Reaction in above 60 group after launch

- As of March 31, 2021, a total of 1,123,413 doses of BIBP COVID-19 vaccine have been administered to people 60 years of age or older in China, 79 cases aged 60 and above were reported;
- Among the 79 cases, 35 cases were mainly general reactions, accounting for 44.30%;
- Followed by coincidental events, with a total of 19 cases, accounting for 24.05%;
- 86% cases have improved or been recovered.

- From the age distribution, the age of the majority of recipients is concentrated in the range of 60-69 years old:
- among them, the age group of 65-69 years old is the most (30 cases); Followed by 70-74 years old group, with 15 cases in total;
- Fewer cases were reported in the age group 75 years and above.

- The 79 AEFI cases reported 125 adverse reaction;
- among which dizziness was the most, with 23 cases;
- Followed by headache and fatigue, with 9 cases each;
- The terms reported more than 5 cases were nausea (7 cases), fever (6 cases), vomiting (6 cases), allergic dermatitis (6 cases), rash (5 cases), palpitation (5 cases),
- the other AEs reported less than 5 cases;

Safety evaluation

AEFI cases are mainly general reactions, followed by abnormal reactions and coincidental diseases.

The known adverse reactions are mainly dizziness, fever, allergic dermatitis, fatigue, etc. The reporting rate of serious adverse reactions is less than 0.1%, which is very rare.

To sum up, the safety profile of Covilo-BIBP in this reporting period are basically consistent with the safety data in the package insert, with good benefits/risks. The company will continue to pay attention to the safety monitoring of this product.

Post-marketing Clinical Studies

Study Code	Subjects	purpose	Location(s)	sample size
CNBG-RWS-001	aged 18 years and above;	effectiveness; safety;	low and middle income countries	At least 526 subjects (70% efficacy)
CNBG-RWS-002	aged 18 years and above;	1. safety monitoring (active urveillance); 2.Special population, Co-morbidities.	China;	1）105,000 subjects (safety)； 2）42,000 subjects ≥60Y； 3）,250 subjects with comorbidity (hypertension and diabetes);
CNBG-RWS-003	aged 18 years and above	1)Immunogenicity 2)safety3）Sepcial populations	China	1,000 subjects
CNBG-CIP-004	aged 18 years and above	Co-administration ：Immunogenicity;safety;immune-interventions;	China	1,152 subjects
CNBG-RWS-005	aged 18 years and above	safety（Passive safety monitoring）； rare/very rare AR； potential ADE/VED;	China	1,000,000 subjects
IVI-006	aged 18 years and above	protective efficacy ； Safety, immunogenicity,special populations； co-administration vaccination;	Mozambique	9,800 subjects;
BIBP2020004CN	aged 3 years and above	Safety, immunogenicity; immune-persistency of different schedules;	China	4400 subjects

Thanks to our collaborators, investigators, subjects and your kindly attention!

- National Medical Products Administration (NMPA)
- Center for Drug Evaluation, NMPA
- Joint Prevention and Control Mechanism of the State Council
- National Health Commission, PRC
- Ministry of Science and Technology, PRC
- National Institutes for Food and Drug Control
- Center for Food and Drug Inspection of NMPA
- Chinese Center for Disease Control and Prevention (CDC)
- Institute of Laboratory Animal Sciences, Cams & Pumc
- People's Government of Beijing MunicipalityManagement Committee of Beijing Economic and Technological Development Zone
- Beijing Municipal Drug Administration
- Henan Center for Disease Control and Prevention
- G42 group
- Al Qarain Primary Healthcare Center
- Shaikh Khalifa Medical City
- Beijing Contrico Statistical Technology Co., Ltd
- Beijing Zhaoyan New Drug Research Center Co. Ltd

Thank you!