Inactivated Vaccine Candidates

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COVID-19 – Inactivated vaccine candidates

	Sinopharm Headquarter: China	Sinovac Headquarter: China
	Sinopharm/Wuhan Institute	CoronaVac
Virus strain	WIV04 strain isolated from a patient in the [redacted (10)(2a)]	CN2 strain isolated from the bronchoalveolar lavage fluid from a patient in [redacted (10)(2a)]
Cell line for virus propagation	Vero cells	Vero cells
Inactivation	β-propiolactone	β-propiolactone
Adjuvant	0.5 mg aluminum hydroxide	Aluminum hydroxide
Buffer	PBS without preservatives	PBS and sodium chloride
Injection	Intramuscular	Intramuscular
Current R&D status	Phase III study ongoing Start: July 2020 Study sites: United Arab Emirates, Peru, Morocco	Phase III study ongoing Start: July 2020 Study sites: Brazil, Indonesia, Bangladesh

Sinopharm – Phase I/II trial

Overview

Phase I trial included 96 participants (18-59 years of age)

- 3 dosage groups: 2.5µg, 5µg and 10µg per dose and aluminum hydroxide adjuvant-only (n=24 each)
- 3 intramuscular injections on day 0, 28 and 56

Phase II trial included 224 participants (18-59 years of age)

- Medium dose (5 µg) given on
  - Day 0 & 14 (n=84; alum only n=28)
  - Day 0 & 21 (n=84; alum only n=28)

Primary safety outcome:

- Combined adverse reactions 7 days after each injection

Primary immunogenicity outcome:

- Neutralizing antibody response 14 days after the whole-course vaccination
- Measured by a 50% plaque reduction neutralization test against live SARS-CoV-2

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Sinopharm – Phase I/II trial

Safety outcomes

- AEs within 7 days after injection were reported by 48 (15.0%) of 320 participants
- Most common were injection site pain and fever
- All AEs were mild, transient and self-limiting

Table 2. Adverse Reactions After 3 Doses in the Phase 1 Trial and 2 Doses in the Phase 2 Trial in the Safety Set[a]

	Phase 1 clinical trial; 0, 28, and 56-d group				Phase 2 clinical trial			
					0 and 14-d Group		0 and 21-d Group	
Adverse reaction	Low dose (n = 24)	Medium dose (n = 24)	High dose (n = 24)	Alum only (n = 24)	Medium dose (n = 84)	Alum only (n = 28)	Medium dose (n = 84)	Alum only (n = 28)
0-7 d								
Total adverse reactions	5 (20.8)	4 (16.7)	6 (25.0)	3 (12.5)	5 (6.0)	4 (14.3)	16 (19.0)	5 (17.9)
Systemic reactions	0	3 (12.5)	1 (4.2)	1 (4.2)	4 (4.8)	2 (7.1)	4 (4.8)	2 (7.1)
Coughing	0	0	0	0	1 (1.2)	0	0	0
Diarrhea	0	0	0	0	0	0	1 (1.2)	0
Fatigue	0	1 (4.2)	0	0	1 (1.2)	0	0	0
Fever	0	1 (4.2)	1 (4.2)	0	4 (4.8)	1 (3.6)	2 (2.4)	1 (3.6)
Headache	0	0	0	0	1 (1.2)	1 (3.6)	0	1 (3.6)
Nausea and vomiting	0	1 (4.2)	0	1 (4.2)	0	0	1 (1.2)	1 (3.6)
Pruritus (noninoculated site)	0	0	0	0	0	0	0	1 (3.6)
Local reactions	5 (20.8)	1 (4.2)	6 (25.0)	2 (8.3)	2 (2.4)	3 (10.7)	13 (15.5)	4 (14.3)
Itching	0	0	0	0	0	0	1 (1.2)	1 (3.6)
Pain	5 (20.8)	1 (4.2)	6 (25.0)	2 (8.3)	2 (2.4)	3 (10.7)	12 (14.3)	4 (14.3)
Redness	0	0	1 (4.2)	0	0	0	0	1 (3.6)
Swelling	1 (4.2)	0	1 (4.2)	0	0	0	1 (1.2)	1 (3.6)
Other reactions	0	0	0	0	0	0	0	0
0-28 d								
Total adverse reactions	5 (20.8)	4 (16.7)	6 (25.0)	3 (12.5)	5 (6.0)	4 (14.3)	16 (19.0)	5 (17.9)

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Sinopharm – Phase I/II trial

Immunogenicity outcomes

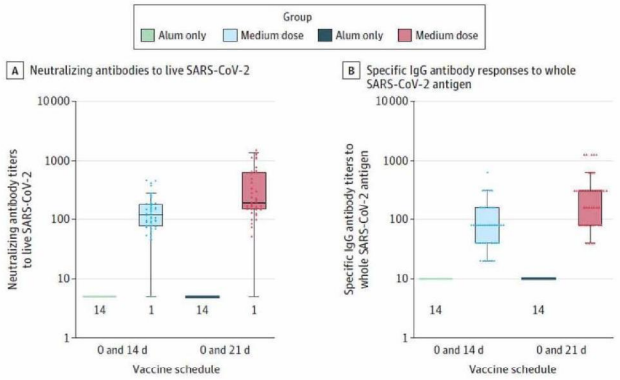
Neutralizing antibody response

- Seroconversion Phase I: 100% in low- and high dose groups; 95.8% in medium dose group
- Seroconversion Phase II: 97.6% in both groups

Specific IgG-binding antibody response

- Seroconversion Phase I: 100% in all groups
- Seroconversion Phase II: 85.7% with 0&14 d schedule; 100% with 0&21 d schedule

Figure 3. Antibody Responses 14 Days After the Second Dose in the Phase 2 Trial



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Sinopharm – Phase I/II trial

Summary

- The inactivated vaccine was well tolerated in all dose groups under different injection procedures
- The incidence rate of adverse reactions (15.0% among all participants) was lower compared with results of other candidate vaccines using other platforms (other platforms mostly >60%, some even 100%)
- No vaccine-related serious adverse events

- The inactivated vaccine induced a robust antibody response
- The results in both phases indicated that a longer interval (21 days and 28 days) between the first and second injections produced higher antibody responses compared with a shorter interval schedule
- Antibody titers further increased after third injection, therefore a booster dose might be necessary

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Sinovac – Phase II trial

Overview

Phase II trial included 600 participants between 18-59 years of age

Schedule:

- Vaccination on Day 0 & 14: 3 μg and 6 μg, or placebo (Participant ratio 2:2:1)
- Vaccination on Day 0 & 28: 3 μg and 6 μg, or placebo (Participant ratio 2:2:1)

Safety analysis:

- Solicited AEs occurring on Day 0~7
- Unsolicited AEs occurring on Day 0~28
- Serious AEs were collected throughout the trial

Immunogenicity outcome:

- Day 0 & 14 schedule: blood samples collected on Day 0, 28 and 42
- Day 0 & 28 schedule: blood samples collected on Day 0 and 56

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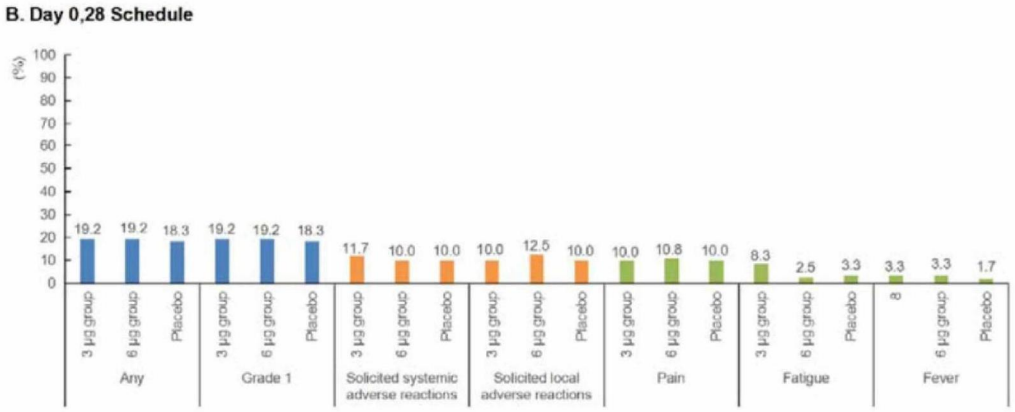
Sinovac – Phase II trial

Safety outcomes

- Most AEs were solicited AEs and mild in severity
- Most frequently local symptom was pain at the injection site (20.3% 0&14 d schedule; 10.3% 0&28 d schedule)
- No grade 3 AEs observed
- During follow up 3 severe AEs were reported from 3 subjects, neither was vaccine-related



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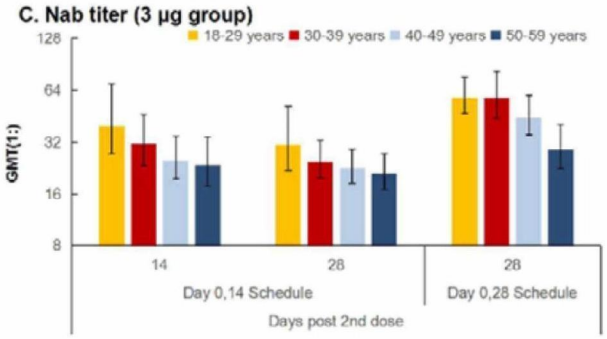
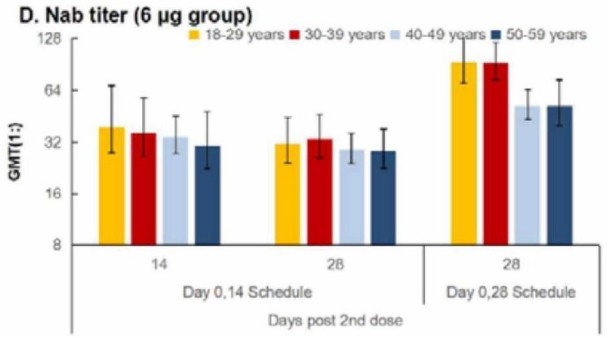
Sinovac – Phase II trial

Immunogenicity outcomes

- Seroconversion rates >90%, no difference between dosage groups and vaccination schedules
- The neutralizing antibody titers and IgG antibody levels were significantly higher after the 0 & 28 d schedule in comparison to 0 & 14 d schedule
- Neutralizing antibody titers decreased with increasing age
  - In both dosage groups (3 and 6 µg) a decrease in Nab levels in the age groups 40-49 and 50-59 was observed
  - Younger subjects tended to have higher levels of Nabs





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Sinovac – Phase II trial

Summary

- Mostly mild adverse reactions, no serious vaccine-related AEs observed
- Incidence rate of AEs comparable between 3µg and 6µg dosage groups
- Compared to other COVID-19 vaccine candidates lower fever incidence rates

- Seroconversion rates in all groups >90%
- Immune response stronger with 0 & 28 day schedule
- Neutralizing antibody titers significantly decreased with increasing age of the participants

Press release from 09-Sep-2020 (unpublished data):

Preliminary results from a Phase I/II trial show good safety and immunogenicity results in adults >60 years of age. 421 elderly volunteers (60-89 years of age) were included in the trial, receiving a two-dose immunization 28 days apart. 3 different vaccine dosage groups were tested.

The seroconversion rate as well as GMT levels for elderly participants were comparable to the adult group aged 18 to 59 years old. All dosage groups were well tolerated.

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http://www.sinovac.com/?optionid=754&auto_id=910


Thank you.
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