The Executive Summary has been replaced with a weekly compendium of items relating to immunity and vaccine development

INTERNATIONAL SOS WEEKLY SCIENTIFIC UPDATE
Focussing on immunity and vaccine development

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In this edition:

1. NOVAVAX TO LAUNCH PHASE 3 TRIALS OF TWO DOSE VACCINE

Features of this vaccine

- Well tested methodology using coronavirus proteins
- Two shots, 28 days apart
- Only needs refrigeration, not deep freeze
- Monkeys protected and high antibody levels found in animal trials
- Some volunteers receiving both COVID and flu vaccines

Animal trials

Twelve monkeys received two doses of the vaccine and were then exposed to the coronavirus. Eleven of the 12 monkeys showed no signs of infection in their noses or lungs. One monkey, which received a low dose of the vaccine, briefly showed signs of infection in the lungs, but all signs of infection were gone two days later.

Phase 1 & 2a results

Phase 1 trials from 131 volunteers showed neutralising antibody levels at more than four times the level of people who had recovered from COVID-19. The vaccine also induced a T-cell response in 16 randomly selected volunteers.

Side-effects

Of the 106 study subjects who received the vaccine, five developed severe side effects, including muscle pain, nausea and joint pain, and one study subject had a mild fever. The side effects lasted, on average, two days or less. Of the 25 volunteers who received placebo injections, three had side effects.

Phase 3 trials

Novavax is about to begin Phase 3 trials in the UK. The study will be in partnership with the UK Government's "Vaccine Taskforce" and will enroll 10,000 volunteers. There will be a special effort to recruit people at high risk, such as healthcare and social care workers. One quarter of the study group will be over 65 years and priority will be given to groups most affected by COVID, including racial and ethnic minorities.

Half will receive two doses of the vaccine: the other half will receive a placebo. Due to the high antibody levels found in earlier phases, it is hoped that the vaccine will have a high efficacy, so smaller numbers of volunteers may be required than in other Phase 3 trials.

More details were given in the Washington Post. A combination of the vaccine and a flu shot will be given to 400 of the volunteers to determine whether it is safe to give the two vaccines at the same time.

The study will end when either 116 people develop symptoms of COVID-19 or 63 people develop moderate to severe COVID-19. The researchers then "unblind" the study and compare how many of the infections were in the vaccinated group compared to the placebo group.

A Phase 3 trial in the US will be run in conjunction with NIH (National Institutes of Health) and will enroll 30,000 volunteers.

Novavax is hoping for at least 60% efficiency – meaning that the vaccine is 60% more effective than placebo.

Vaccine details
Novavax is a "sub-unit" vaccine. Fragments of the virus, such as the spike protein, are used to invoke the immune response. The vaccine includes Novavax' proprietary MatrixM™ adjuvant. Adjuvants are used in vaccines to create a stronger immune response.

The vaccine can be stored between 36 and 46 degrees F (2 – 8 degrees C) and thus can be distributed using standard vaccine channels.

Vaccine supply
Novavax has contracts with several manufacturing partners, including the Serum Institutes of India. It predicts it will be able to make several billion doses per year.

Vaccine purchase
The UK has agreed to buy 60 million doses of the Novavax vaccine.

US Government investment
The New York Times states that the US Government's Operation Warp Speed Program has invested about $1.6 billion in the Novavax vaccine development. To date, the program has invested over $10 billion in private companies' coronavirus vaccines.

Other vaccines soon for Phase 3 trials
Sanofi has a vaccine candidate that is likely to start Phase 3 trials soon.

2. UPDATE ON CHINESE VACCINES

The South China Morning Post (based in Hong Kong) has reviewed the progress of Chinese COVID-19 vaccine development.

Main points

- Four Chinese vaccines are in Phase 3 trials

- China began vaccinating selected workers in July
- Chinese vaccines may have a high price tag
- China has promised vaccine to a significant number of countries

The Chinese vaccine manufacturers with vaccines in Phase 3 trials

- Sinovac Biotech (1 inactivated vaccine)
- CanSino Biologics (1 adenovirus vector vaccine)
- CNBG: (China National Biotec Group) - (2 inactivated vaccines)

China began vaccinating in July

- China approved three inactivated vaccines for emergency use in July 2020
- Recipients include medical staff and border inspection officials
- No serious side-effects have been reported
- Entry to the mass market is dependent on the results of the Phase 3 trials

Production capabilities

- The National Health Commission (NHC) says China will be able to produce 610 million doses of vaccine in 2020
- In 2021 China will produce 1 billion doses

What will Chinese vaccines cost?

- CNBG's Vice-President has said that, if approved by the drug regulator, its vaccines would be available for a maximum of 600 yuan (USD$88)
- Both AstraZeneca and Johnson & Johnson have cited lower prices for their vaccines
- AstraZeneca has said that its vaccine will cost about USD$4 per dose when sold to the US Government.
- Other countries are buying AstraZeneca vaccine at an undisclosed price

Not all in China will be vaccinated

- There is no current plan for universal vaccination
- The vaccination program will start with high-risk groups, including border agents and medical workers as well as the elderly, pregnant women and children

Which countries will receive Chinese vaccine?

China is not participating in the WHO COVAX program.

- President Xi has said African countries would be among the first to benefit
- Countries where clinical trials are running could be early recipients:
    - UAE / Bahrain / Peru / Morocco / Turkey / Bangladesh / Brazil / Indonesia
- Priority is also being given to the "Mekong River" countries:
    - Cambodia / Laos / Myanmar / Thailand / Vietnam
- The Philippines has been promised early access
- Loans are available to Latin American and Caribbean nations to purchase vaccine

Chinese manufacturers will apply for the US FDA licensing if they pass Phase 3 trials

- Sinovac will apply to the US Food and Drug Administration to sell its vaccine in the US if it passes its Phase 3 trials
- Sinovac will also apply for EU licensing

3. MODERNA UNABLE TO APPLY FOR EUA UNTIL AT LEAST 25 NOVEMBER

The Financial Times reported that Moderna Chief Executive Stéphane Bancel would not be able to apply for Emergency Use Authorisation (EUA) of its COVID vaccine until late November. He also said that he did not expect to have full approval to distribute the vaccine to all sections of the population until March 2021, at the earliest.

Moderna vaccinated the 15,000th participant in its 30,000-person trial on 26 September making 25 November the earliest it could complete two months of screening after the second dose; this is an FDA (US Food and Drug Administration) requirement.

4. BioNTech / PFIZER VACCINE SHOWS GOOD ANTIBODY AND T-CELL RESPONSE

Nature (in an unedited manuscript) has published results from BioNTech / Pfizer Phase I/II trials. The BNT162b1 vaccine elicited strong antibody and CD4 and CD8 T-cell responses after two doses in trial in healthy adults, 18-55 years of age. IgG concentrations were higher than in a COVID-19 human convalescent sera.

International SOS Comment: This shows that the Pfizer vaccine has strong immunogenicity in healthy adults. We await similar trials in older subjects and efficacy data.

5. DOCUMENTED REINFECTIONS CAN BE MORE SEVERE THAN ORIGINAL COVID-19

BNO News has a "reinfection tracker" that so far has documented at 22 cases of genomically confirmed COVID-19 reinfection. Confirmation of reinfection requires two episodes of COVID, each caused by a SARS-CoV-2 virus having a different genetic makeup.

In the 12 cases where severity data had been documented, the second cases were:

- Less severe in three cases
- The same severity in one case
- More severe in eight cases, with three of these being severe

International SOS Comment: More studies and data are required however the assumption that a second case of COVID-19 would be less serious than the first may not be valid.

6. FDA WIDENS U.S. SAFETY INQUIRY INTO ASTRAZENECA CORONAVIRUS VACCINE

Following the report on 6 September of a possible serious side-effect, believed to be a rare spinal inflammatory disorder called transverse myelitis, the Oxford / AstraZeneca vaccine trials were put on hold globally. Regulators in the UK, Brazil, India and South Africa subsequently allowed the trials to resume.

However, the trials have remained on hold in the US and Reuters reports that the FDA (Food and Drug Administration) has widened its investigation; it will look at data from earlier trials of similar vaccines developed by the same scientists. This may lead to additional delays for the vaccine.

AstraZeneca, in a statement, said: “We are continuing to work with the FDA to facilitate review of the information needed to make a decision regarding resumption of the US trial.”

7. POSSIBLE NEEDLE-FREE COVID-19 VACCINE ADMINISTRATION

The Conversation reports that Australian Government has provided funding to the University of Sydney to begin human trials using a “liquid jet” injector to deliver its DNA-vaccine. Liquid jet injectors use small volumes of liquid forced through a tiny opening (smaller than a human hair). This ultra-fine high-pressure stream penetrates the skin where cells then take up the vaccine and stimulate immune cells.

This method was effective in several clinical trials against HIV and is currently used to deliver some influenza vaccines. Both RNA and DNA coronavirus vaccines may be suitable for this delivery method

8. STRONG CELLULAR IMMUNE RESPONSE TO SARS-COV-2

“Understanding which arms of the immune response are responsible for protection against SARS-CoV-2 infection is key to predicting long-term immunity and to inform vaccine design. Two studies in this issue of Cell collectively suggest that, although SARS-CoV-2 infection may blunt long-lived antibody responses, immune memory might still be achieved through virus-specific memory T cells.”

The two studies demonstrated “potent memory CD8+ and CD4+ T-cell responses were elicited during asymptomatic infections, even in the absence of detectable antibody responses.

“This increases the likelihood of protective immunity post-SARS-CoV-2 infection.

“However, robust memory CD8+ T cell responses may be difficult to recapitulate with vaccination, which will likely be more reliant on the induction of potent high-affinity neutralizing antibodies.”

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