INTERNATIONAL SOS WEEKLY SCIENTIFIC UPDATE
Focussing on immunity and vaccine development

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13 November 2020

In this edition:

A. Vaccine Development & Approval

1. Russia says its Sputnik V COVID-19 vaccine is 92% effective

Russia’s Sputnik V vaccine is 92% effective at protecting people from COVID-19 according to interim trial results, the country’s sovereign wealth fund said on Wednesday. The trials evaluated efficacy among over 16,000 volunteers who received the vaccine or placebo.

A statistical analysis of 20 confirmed cases of coronavirus indicates that the Sputnik V vaccine had an efficacy rate of 92% of preventing COVID-19 after the second dose.

Requests for more than 1.2 billion doses of Sputnik V vaccine have come from over 50 countries. The vaccine supplies for the global market will be produced by international partners in India, Brazil, China, South Korea and other countries, and should enable the production of 500 million doses of the Sputnik V vaccine outside Russia annually. Further increases to the foreign production capacities are being considered.

In addition, the Argentinian Government will purchase 25 million doses of the Russian Sputnik V vaccine between December and the first half of January if Phase 3 results are positive.

2. Medicago and GSK testing vaccine using virus-like particles from tobacco plant

Canadian biopharmaceutical company Medicago and GSK are entering Phase 2/3 trials with their coronavirus vaccine candidate which uses recombinant spike (S) glycoprotein expressed as virus-like particles (VLPs) grown in a close relative of the tobacco plant. The vaccine combines the particles with GSK's adjuvant to generate an immune response. The Phase 1 results were encouraging and supported further clinical evaluation.

The Phase 2 trial will be conducted in multiple sites in Canada and the US. The volunteers will include healthy adults ages 18 to 64 and elderly adults over 65. Each age group will include more than 300 subjects.

3. Fosun to launch BioNTech / Pfizer COVID-19 vaccine in China

Fosun, one of China's biggest private-sector conglomerates, will pay up to US$135 million towards the development and registration of Pfizer / BioNTech vaccine, reports the South China Morning Post. Fosun hopes to launch the vaccine in China, Taiwan, Hong Kong and Macau at the same time as it is released in the US and Europe.

Following the release of the interim analysis results indicating that the Pfizer / BioNTech vaccine may prevent up to 90% of COVID, Fosun hopes to launch the vaccine in China after going through a bridging trial. The number of volunteers required for the bridging trial in China will be much smaller than trials conducted overseas.
A bridging trial is designed to demonstrate equivalent immunogenicity i.e. exclude a clinically significant difference in the immune response between the population in whom efficacy was shown and the population to whom those efficacy results are extrapolated.

4. Australia has begun production of AstraZeneca/Oxford vaccine

Australian vaccine manufacturer CSL reports starting producing University of Oxford and AstraZeneca candidate vaccine on 9 November. The production of the Oxford vaccine comes before it has been approved by the Therapeutic Goods Administration (TGA).

The New Daily states that the vaccine candidate developed by the University of Queensland (UQ) is also in production by CSL. The UQ vaccine is undergoing Phase 1 trials.

Australia had previously confirmed an order for 51 million doses of the UQ vaccine and 34 million of the Oxford candidate.

Australia has also recently announced deals to purchase the Novavax and Pfizer / BioNTech COVID vaccines

5. CEPI to provide millions of dollars for Chengdu-based vaccine firm

Chengdu-based vaccine maker Sichuan Clover Biopharmaceuticals will receive up to US$328 million from CEPI (Coalition for Epidemic Preparedness Innovations), an Oslo-based organisation working with the WHO on international vaccine access, Reuters reports.

Clover will begin phase 2/3 trials of its "S-Trimer" experimental vaccine and scale up manufacturing to about billion doses a year. Clover and GlaxoSmithKline (GSK) have been conducting Phase 1 trials using a GSK adjuvant (vaccine booster).

If proven safe and effective, the Clover vaccine will be available through COVAX, a WHO program planning to equitably distribute two billion doses of COVID-19 vaccines to various participating countries by the end of 2021. CEPI is one of two WHO partners leading the programme. Oslo, Norway-based CEPI was set up in 2017 to fight emerging epidemics and is backed by 14 governments, the Bill and Melinda Gates Foundation and Britain's Wellcome Trust. CEPI has supported COVID-19 drug developers including Inovio Pharmaceuticals, Moderna, and Novavax.

6. Europe will not set a minimum level of efficacy for COVID-19 vaccine candidates

Europe's drug regulator, the European Medicines Agency (EMA) has said that it will not set a minimum level of efficacy for potential COVID-19 vaccines when considering them for approval, reports Reuters. The EMA will consider all data on each candidate. This is a different approach to that of the FDA (US Food and Drug Administration) that has said that a vaccine must have a minimum efficacy of 50% to be considered for approval.

B. Vaccine Distribution

1. Australia to use "Eskies" in cold chain logistics for Pfizer mRNA vaccine

On 11 November, "Greg Hunt, Australia's Health Minister, announced Australia had secured 'full cold chain logistics' distribution for the Pfizer vaccine, meaning vials could be transported where needed," reports The New Daily.

"The vaccines will be stored in carriers that Therapeutic Goods Administration (TGA) head John Skerritt referred to as 'very sophisticated Eskies', which require dry ice."

- An Australian "Esky" is a portable insulated container with provision for packing food and drink in ice.
- Cultural translation of Australian Esky: USA - Cooler, NZ - Chilly bin, UK - Cool box.

2. UK GPs on standby for December vaccination program

NHS England has written to GPs asking them to prepare for a possible December coronavirus vaccination programme.

NHS England Chief Executive, Sir Simon Stevens has told a news conference that the NHS would also require "roving teams" who will prioritise care homes and social care staff, and other vulnerable groups. In addition the "Nightingale Vaccination Centres" are being set up. Sir Simon said that the NHS is planning in case some vaccine to available before Christmas.

C. Outbreaks and Epidemiology

1. CDC: Pregnant Women Face Higher Severe COVID-19 Risks

Pregnant women who contract the coronavirus are more likely to develop a severe form of the disease, die from COVID-19 and/or deliver prematurely, according to new studies released by the CDC.

The CDC emphasized that the overall risk remains low however pregnant women face a "significantly higher" risk for severe consequences. "Pregnant women should be counseled about the risk for severe COVID-19-associated illness including death."

D. COVID Testing

1. Point-of-care T cell testing has implications for tracking exposure & vulnerability

Adaptive Biotechnologies, a Seattle-based company, has developed a point-of-care T cell test, reports the New York Times.

In an initial study, researchers from Italy, the United Kingdom and the United States studied people in Vo (the town where the virus first spread in Italy) to learn more about testing accuracy. Blood tests were performed on 70 people who had had confirmed cases of coronavirus about two months earlier.

Theoretically, all 70 should have had positive results for antibodies, but these were negative in 16 of the 70, or 23%. The T cell test missed only two cases or about 3%.

Adaptive Biotechnologies will be applying to the FDA (US Food and Drug Administration) for an EUA (Emergency Use Authorization) for its point-of-care T cell testing.

"'This makes sense. It's well known that antibodies wane, but T cells have immunological memory,' said Dr. Peter Hotez, an infectious disease specialist at Baylor College of Medicine," on CNN.com.

The data was announced 10 November at an investors' call for Adaptive Biotechnologies. The company did not fund the study and the data has not been published.

E. The Pfizer coronavirus vaccine works! What else do you need to know?

The announcement by Pfizer and BioNTech on 9 November was the first solid evidence that a vaccine can prevent COVID-19. However, there are details about protection provided by the vaccine that remain unanswered.

About the vaccine and the trial

How does an mRNA vaccine work?

- Part of the coronavirus gene (mRNA - which codes for the virus spike protein) is injected into the body
- The body's cells use the RNA to create spike protein antigens
- The body develops an immune response against the spike protein of the coronavirus

How is the vaccine stored?

- mRNA vaccines must be stored at -70C (temperature of dry ice). Prior to administration, they can only be stored at 4C for 24 hours

How was the trial set up?

- > 44,000 volunteers were divided into two groups (both received two injections 21 days apart)
  - 50% received vaccine, called BNT162b2
  - 50% received an inactive injection (placebo)

- This is a “double blind trial” - neither the volunteer nor trial staff know who received vaccine and who received placebo

What has the Interim Analysis told us?

What is an “Interim Analysis” (IA)?

- An “Interim Analysis” is a specified point in a trial when some interpretation of the results is allowed
- In this IA of the Pfizer trial, 94 volunteers in the trial had developed laboratory-confirmed COVID
- The trial is “un-blinded” for the 94 who developed COVID to determine who had received vaccine and who had received placebo

Results

- Pfizer did not provide the number of people in each group who developed COVID
- However, an independent board of experts interpreted the results as indicating that the vaccine is > 90% effective at preventing COVID – however the final vaccine efficacy percentage may vary
- Note: the trial continues until 164 people in the trial have developed COVID

The vaccine appears to be safe

- So far Pfizer and BioNTech have reported no serious safety concerns from their vaccine

What don’t we know?

What types of COVID can the Pfizer vaccine protect us from?

This IA does not provide details of the severity of COVID-19 prevented:

- Mild? / Moderate? / Severe?

Age groups protected?

- The IA does not specify the age groups that were protected, however people aged 12 – 85 have been included in the trial

Other groups protected?

- The IA does not specify if other risk groups were protected (or excluded from the study) but does say that 42% of participants had racially and ethnically diverse backgrounds

Lasting immunity?

- The Pfizer Phase 3 trial has not been running long enough to provide information on the duration of immunity
- However, duration of immunity may be able to be derived from volunteers who participated in earlier Phase 1 & 2 trials (and thus were vaccinated several months ago)

What may this indicate about other vaccines?

Due to the positive Pfizer result, we are generally more confident that:

- Other mRNA vaccines will work (Moderna: IA results expected soon)
- Other vaccines creating an immune response to the spike protein will work (includes the "viral vector" vaccines such as Oxford/AstraZeneca, Johnson & Johnson and CanSino)

What are the next steps for Pfizer?

Trial continues

- The Pfizer trial will continue at least until 164 volunteers have developed COVID-19
- The results will then be re-analysed

Authorisation for use

- Pfizer will apply to the FDA (US Food and Drug Administration) for an EUA (Emergency Use Authorisation) in 3rd week in November

The future of the Pfizer and other vaccine trials

1. If a vaccine, such as Pfizer, is found to be very effective, at some point the trial will be stopped and the vaccine given to the volunteers in the placebo arm of the trial

2. For vaccines that are yet to start Phase 3 trials, the placebo arm of the trial may be replaced with a successful vaccine (e.g. Pfizer) and so the new vaccine is tested against this successful vaccine. This is a so called "non-inferiority" trial.

Availability

- The Pfizer vaccine is unlikely to be widely available until well into 2021

References:

Nature
Chemical & Engineering News
Forbes
AMA interview with Dr Fauci (highly recommended)
New York Times