Development of potential COVID-19 vaccines continues to accelerate

Never before has the world come together as it has to find a vaccine and treatments for COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). At the time of writing (June, 2020) multiple vaccine candidates are in phase 1, 2, and 3 trials, while other promising candidates are finishing their preclinical trials. An update on four of these candidate vaccines is provided here.

One candidate that could be among the first to cross the finish line—and that is certainly receiving huge media attention—is the recombinant vaccine AZD1222 from the University of Oxford and AstraZeneca, in which a replication-deficient chimpanzee adenovirus is used to carry DNA for the spike antigen protein of SARS-CoV-2 that enables the virus to infect human cells. Due to the immunogenicity of adenoviruses, it is hoped this vaccine could provide better protection with fewer doses than some of its rival candidates.

The Oxford team was able to pull ahead in the race for a vaccine because it had already completed safety testing on a similar vaccine candidate in 2019, for Middle East respiratory syndrome coronavirus. AZD1222 has now entered phase 2 and 3 trials in the UK, although decreasing transmission in the UK means efficacy might need to be assessed in other phase 3 trials later this year in Brazil.

Also in the UK, the Imperial College London team led by Robin Shattock has received more than US$50 million in UK Government funding to accelerate its efforts to produce a vaccine using novel self-amplifying RNA technology developed by Shattock himself over several decades—a technology that has not yet produced a vaccine. The vaccine is made of RNA that instructs muscle cells in the body to produce the distinctive spike protein present on the surface of SARS-CoV-2. It is hoped these proteins will trigger an immune response that would then be able to kill the virus. At the time of writing, a combined phase 1/2 trial with 300 participants in the UK is underway. If shown to be safe, the vaccine will enter phase 3 trials in October, in a country where community transmission remains high.

As with Imperial College, the mRNA-1273 vaccine by Moderna (Cambridge, MA, USA) has been created using mRNA technology yet to be used in vaccine production. A phase 1 study of eight participants reported in May, 2020, produced an immune response with levels of neutralising antibodies similar to those seen in people previously infected with COVID-19. A phase 2 study of this vaccine with 300 adults and 300 older adults (aged 55 years or older) has now been fully enrolled, and Moderna has announced its future phase 3 trial will involve 30 000 participants across the USA and will be run in conjunction with the US National Institute of Allergy and Infectious Diseases (UNAID), headed by Anthony Fauci. The company, which has received almost half a billion US dollars in US Government funding, says it is on track to be able to produce 500 million to 1 billion doses by the start of 2021.

Shattock has said that Imperial's vaccine would require a dose 50–100 times smaller than the Moderna vaccine, substantially lowering the potential cost. Manufacturing facilities for the Imperial vaccine could also be smaller and cost less than those producing the other candidate vaccines. Meanwhile, AstraZeneca, which has received substantial funding from the US and UK Governments and the Centre for Epidemic Preparedness and Innovation (CEPI), has agreed to distribute the Oxford University vaccine at cost. The company has secured capacity to produce 2 billion doses of its vaccine, including 400 million for developing countries, by the end of this year.

Elsewhere, CEPI has also invested almost $400 million in the vaccine development efforts of Novavax (Rockville, MD, USA). Theirs is a protein subunit vaccine, in which proteins are encased in a nanoparticle that gets injected along with an adjuvant. A phase 1 trial of 130 volunteers is ongoing in Australia and is expected to report in July, 2020. Should this trial be successful, a phase 2 study will then be done in multiple countries including the USA. CEPI has said that it will further support the vaccine to licensure, if the results are positive. The sponsorship also includes a deal to transfer technology to partners across different regions for large-scale production, as well as plans to ensure equitable global access.

Researchers at WHO and UNAID are among those considering human challenge trials for vaccine candidates, in which vaccinated individuals are directly exposed to the virus to establish efficacy, rather than relying on the changing dynamics of the pandemic in different countries. However, questions remain over the ethics of this approach, even in the middle of a global pandemic that has already killed hundreds of thousands of people, and ultimately, equitable access to a vaccine will depend not only on which vaccines are finally approved, but the order in which they attain approval. And currently, none of the parties involved in this process can provide the most important guarantee—that we will definitely be able to produce a vaccine that protects against COVID-19.

Tony Kirby

For more on the **AZD1222 vaccine** see https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-advances-response-to-global-covid-19-challenge-as-it-receives-first-commitments-for-oxfords-potential-new-vaccine.html and http://www.ox.ac.uk/news/2020-05-22-oxford-covid-19-vaccine-begin-phase-iiiii-human-trials

For more on **vaccine developed at Imperial College London** see https://www.imperial.ac.uk/news/198314/imperial-begin-first-human-trials-covid19/

For more on the **mRNA-1273 vaccine** see https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-positive-interim-phase-1-data-its-mrna-vaccine

For more on the **vaccine developed by Novavax** see https://ir.novavax.com/news-releases/news-release-details/novavax-receive-388-million-funding-cepi-covid-19-vaccine