Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #58

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Salvagene SARS-CoV-2 Task Force:

The Salvagene SARS CoV-2 Task Force one year on – Salvagene introduces infection and vaccination log for Premium clients.

KEYNOTE

Dear Premium Customers,

On 20th January 2020, we set up our Salvagene SARS CoV-2 task Force with the purpose of ensuring that Salvagene clients receive the best possible standard of service during the current crisis.

This last year has gone by surprisingly fast for us, and it seems like only yesterday that we were putting our team together. Almost six weeks before the World Health Organization declared the pandemic, the data we had already received from Asia prompted us to react at a relatively early stage. It was a very busy time for us, during which we learned a lot. Looking back at all of our communications with you during these past 12 months, we have published around 100 Keynotes and at least as many podcasts. They are still all available online as well as on our app. Somewhat to our surprise, none of these communications has turned out to be wrong in terms of content. We have no regrets as to the information we have published here, because we pride ourselves on taking a very clear approach and see ourselves as a filter to minimize the spread of “fake news”.

From the beginning, we have been cautious in all our pronouncements on the virus because we were conscious of how little anyone knew about it. Admittedly, even one year later, our knowledge remains limited. Regrettably, some of the measures that we thought would make a sensible contribution have not been implemented. For example, a stronger focus on antibody rapid tests for home use, which we identified as a potential game-changer many months ago. If only a fraction of the approximately 12 trillion dollars that the major central banks have printed to deal with the economic damage caused by the crisis or even a small part of the billions spent on developing vaccines had gone into such a project, then the pandemic could have been handled with much greater cost efficiency. The economic damage would be less severe and, moreover, it would have provided the breathing space to perfect a sustainable and efficacious vaccine.

Unfortunately, this did not happen, and the exclusive focus on vaccine development could yet have dire consequences. In particular, the mutation events we predicted are now occurring, with the consequence that vaccines, if developed too early, may be less effective up to the point where they have zero efficacy. They may even have the unintended consequence of fueling mutation. At the moment we are dealing with Escape Mutants, where the point is when completely vaccinated people fall ill. In this case, sequencing must be carried out immediately. In addition, the vaccines currently on the market do not provide full sterile immunity, a weakness that is especially true of AstraZeneca.

We know that when you have an acute respiratory viral illness such as Covid-19, drug therapy becomes problematic. By the time you realize that you have contracted the virus, it has already taken off, at which point, of course, an antiviral drug is not going to have much effect.

For almost eight months now, our Vaccine Advisory Board has been keeping track of vaccine and drug developments and posting its findings on our website. In the area of medication, there have been many initiatives, but so far without conclusive results. This applies equally to antivirals and antibody therapies, although we see good prospects for the latter. The one drug that has shown promising results is dexamethasone, although this does not act on the virus itself but rather on moderating the immune reaction. Again, we advise against taking standard supplements or vitamins as a preventive measure, the main danger here being that they may provoke an excessive immune reaction (cytokine storm) in the event of infection.

Overall, we have been impressed by the speed and efficiency with which vaccines based on adenoviruses and mRNA have been developed within the short period of 12 months. Because we are at home in the field of cancer prevention and genetic engineering, we were less surprised by the success of the mRNA projects. It was already clear to us that this technology had potential, although we could not have foreseen just how timely it would be.

We have already described the advantages of mRNA in previous Keynotes. Whenever vaccine-resistant variants emerge – and we have to assume this will be the case on the basis of current developments – then the mRNA vaccines in particular will be adapted relatively quickly. BioNTech has already started to develope an improved version against the Corona variants, according to *Reuters*.

We continue to hold back in making any comprehensive recommendations on vaccination. So far, we have only been in contact with a limited number of Premium clients who have been identified by the Salvagene A.I. Program as having high Covid-19 risk factors.

Looking back on the first year of the pandemic, it has to be said that the politicians and certain sections of the scientific community totally ignored the possibility that the virus might mutate. We addressed this issue in our Keynotes as early as March 2020. This has proved to be a major error with potentially enormous consequences.

We see it as part of our scientific approach here at Salvagene to filter out the wishful-thinking factor and to make purely fact-based forecasts using A.I. technology. Let us suppose that a crucial mutation happens in every 10,000 patients, in which case it won't matter too much as long as only 100,000 people become infected. At the moment, however, we have more than 100 million infections worldwide. Even with a slow-mutating virus, it is obvious that serious mutations are going to develop.

Our prediction is that there will be significantly more mutations, including some that have already happened but so far gone undetected because of the woeful lack of sequencing around the world. Even more serious mutations than those discovered to date cannot be ruled out. Fortunately, there are a few countries such as the UK where genetic sequencing is taken seriously. The problem is that the work they do enjoys hardly any scientific esteem despite its importance for public health. In the UK, 30,000 people are currently being randomly selected to have a smear test which is then sequenced. This is an incredibly valuable study that puts the country in the vanguard of research.

If we had a strong global organization able to play a coordinating role – for which the WHO would seem to be the obvious candidate – the strengths of the different countries could be pooled. As we see it, this would be a much more effective way of dealing with the pandemic, focusing on the strengths of each country rather than its weaknesses. For example, the UK is a world leader in genetic sequencing but displays severe flaws in other areas. Another example is Israel, which could serve as a role model in its vaccine rollout program but has had disastrous practices in other areas.

And then there is Germany, the country where by far the two best vaccines (both mRNA-based) have been developed – BioNTech and CureVac, the second of which is about to be approved – but a country in which management at federal government level has been inadequate. Asian countries have set standards in pandemic countermeasures and tracing. The USA has made a number of poor decisions but did at least implement our favored intermediate solution, namely antibody rapid testing. Unfortunately, the program was not systematically pursued. If these strengths were coordinated worldwide, the overall situation would look a lot better.

At the beginning, a lot of time was lost because the transmission pathways were not properly recognized. Here too, we provided comprehensive information at an early stage on the danger posed by aerosols. We see a clear difference to rhinoviruses and adenoviruses which, in contrast to SARS CoV-2, have no envelope. It was therefore apparent to us from the start that the novel coronavirus was similar to the ones responsible for influenza which are transmitted via contact as well as via droplet infection. Back in April of last year, we were nonetheless very surprised by the dominance of droplet infection.

With mutant forms now having come to prominence and because this is our area of specialism, we are beginning to become more involved. We are working on the assumption that the pandemic will only reach its peak sometime during the current year. We can speak of a virus's "arsenal of weapons" which, by its very nature, lies in its ability to mutate. It is only now, in 2021, that we can see how this confrontation will pan out. We think that the decisive battle will not be fought until autumn in the northern hemisphere.

There are two reasons for this:

1) The infection rate in the southern hemisphere during their summer is currently already very high. We assume that, even if the countries in the northern hemisphere achieve a high

penetration of vaccination by October, the movement of people from the south to the north will again increase infections significantly, thereby introducing their mutations.

2) Furthermore, we assume that the mutations that will emerge in the next few months will create a race against the vaccine in the northern hemisphere, as in Israel at the moment. We see the virus as having a clear advantage. In this respect, there is a possibility that resistance will develop, that vaccines will not have the same efficacy as in the Phase 3 trials. And as a result, we will constantly be on the back foot in terms of vaccine development and the pandemic measures we introduce.

With the appearance of the very first mutations, we see that AstraZeneca has stopped vaccine production. The real reason is that the AstraZeneca vaccine needs to be adapted to the B.1.1.7 variant, and the scientists therefore want to conduct a study to redesign the vaccine first. This is why the vaccine supply targets promised to the EU cannot be met.

We assume that, in addition to the B.1.1.7. variant, the 501Y.V2 variant and the three different B variants from Brazil will also be included. The EMA is expected to grant approval to the AstraZeneca vaccine. There might be a resctriction for persons over 65 years of age. This will be decided this Friday.

This is why, as already mentioned, we have been reticent in making recommendations on vaccination. It remains unclear to what extent a booster jab will be effective against a new variant if the first dose was administered at too early a stage. Irrespective of the reservations we have expressed, we would nonetheless argue that, for overall management of the pandemic, it is important for as many people to get vaccinated as soon as they can. However, this may not necessarily coincide with the best interests of our clients at the personal level.

In the coming days and weeks, there are three keys questions that have to be answered – for us, for our clients and ultimately for every single person on the planet.

The vaccines currently available are BioNTech, Moderna, AstraZeneca and – to a lesser extent – Sinovac and Sinopharm from China, as well as Sputnik V from Russia. They will soon be joined by CureVac from Germany. No other candidate will come into contention for several months yet, either because they are not yet ready for market launch, or because they come nowhere near matching the performance of the first three listed above. Some of the earliest vaccine projects have meanwhile been abandoned, such as Merk in the USA.

The three central questions are as follows:

1) Does vaccination guarantee sterile immunity, i.e. is a vaccinated person still infectious?

With our current state of knowledge, we cannot answer this with certainty. In the specific case of AstraZeneca, however, it is a clear "No", as statements from AstraZeneca itself and from the UK National Health Service confirm and as we ourselves posted in some detail on our app. We suspect that Moderna and BioNTech will also not achieve full sterile immunity. We will continue to monitor the situation. We are currently skeptical about the feasibility of governments issuing vaccination passports.

2) Are the vaccines also effective against the new mutants?

These two questions are of vital importance, both for the individual who is vaccinated and for society as a whole in its efforts to manage the pandemic. As far as BioNTech is concerned, we have already had sight of four studies that say more or less the same thing, two from BioNTech itself, one from the University of Texas and one from a Dutch university

consortium. These state that the vaccine is effective against the B.1.1.7 variant, although efficacy may be slightly compromised. As for the 501Y.V2 and Brazilian B variants, we cannot say either way at present.

No official studies have been published by Moderna on the variants mentioned above – only an internal, small-scale laboratory experiment, the results of which have not yet been made public. The CEO of Moderna has issued a press release stating that neutralizing antibodies are produced against the mutants "to a sufficient extent", that "similar numbers" of antibodies are produced, and that he "presumes there is protection". Because of the uncertainty surrounding the Moderna vaccine, we consider this to be only a second-best option after BioNTech. We are also concerned about some cases being reported from California and Norway that have not yet been clarified.

At AstraZeneca, it has now become clear that the vaccine is significantly less effective against B.1.1.7. Production has been scaled back in order to possibly adjust the vaccine.

3) <u>What are the consequences of the mutants known so far?</u>

With the B.1.1.7 variant, we have seen evidence that it is significantly more transmissible and – more recently – that it may have a slightly increased mortality rate. There are suppositions and conjectures that have not yet been conclusively assessed.

The transmissibility of the South African and Brazilian variants is also significantly higher. But the crucial aspect is that both variants have the E484K mutation and thus lead to significantly more severe symptoms and outcomes for younger people.

E484K stands for the mutation of glutamate (E) and lysine (K) at spike protein site 484. The name of this variant is heard more and more frequently. It appears that vaccines may be less effective against forms of the virus with this mutation. Consequently, E484K complicates the entire vaccine strategy. It is at least partially able to escape the efforts of the immune system to prevent the virus penetrating the cell. This was established by the research team at Rockefeller University in New York. In some of their samples, the antibodies were only one third effective against the virus. That is a significant gap. We concur in their conclusion that the antibody response varies in defending against the virus. There is also supporting evidence from Brazil and South Africa. As we noted in Keynote 56, the authorities in Manaus thought that a degree of herd immunity had been achieved, but the city was then overwhelmed by a massive new wave of disease brought on by the mutant form. This has brought the health system back to the point of collapse. There is, of course, still the prospect of immunity through vaccination, which offers a relatively good level of protection.

The South African variant with 501Y.V2 (which has recently also been given the name B.1.351) will spread very vigorously, similar to the B.1.1.7 variant. It has already appeared in the Caribbean.

Looking ahead to the next few months, we suspect that there will be a lack of transparency around the world regarding developments in immunity among individuals who have already been infected once. We think that this will not last as long as people had hoped. There has been a sharp increase in the number of infections, especially in countries where the mutant forms have already spread. The antibodies developed to ward off the original variant do not help much; in fact, it may even be the case that these antibodies are counterproductive because they trigger problems at the spike protein. There have already been examples of this: in Germany, an individual was infected twice within just a few weeks and had the B.1.1.7. variant in the second infection.

This shows that the antibodies of the initial infection probably do not work against reinfection with a different variant.

Because of the aforementioned problems with the vaccines and their effectiveness against the various mutants, we have now launched an infection and vaccination log for our Premium clients. In the event of an infection, we record when it occurred, when approximately it ended, together with the consequences which we then monitor as part of our aftercare protocol. This gives us the advantage of having enough knowledge to be able to react better in case of multiple infections.

The same applies to Premium clients who have been vaccinated. Here, the date on which the injection was given is crucial, because we need to know which version of the vaccine from which manufacturer was given in which country. We predict that the biggest test will come in the autumn of this year, when there will be a new wave of infections with new mutants. We will then be able to see what the situation is and take preventive action.

It is important for us to obtain the following data from our clients in order to offer the best possible standard of service based on the conclusions we draw in the coming months about the SARS CoV-2 mutations and also developments in vaccine production.

If you become infected – or indeed you suspect that you may have been infected – please report this to us immediately. We will then monitor you during the infection phase and, at the end when a negative PCR test is forthcoming, we will proceed directly to the aftercare phase, by which time it may also be possible for us to establish which mutant the client has been infected with.

The same applies to vaccination. Ideally, we need to know exactly when inoculation took place, with which vaccine, and in which part of the world. This is because the vaccines also differ in part due to different production procedures at the various sites, and due to the timing, the batches are also different or, as is the case now with AstraZeneca, there are different vaccine versions.

The first hours after infection are the crucial phase, especially when the interferon receptors, which we regularly test in the course of our C19 Immunization Program, are not fully active. If the immune response, in particular antibody production, is delayed in this early sensitive phase, it may allow complications such as embolisms, thromboses and blood poisoning to arise without symptoms manifesting themselves. Once that has happened, the options for intervention are limited. As things stand at present, the only treatment available is dexamethasone. To avoid this chain of events, we rely on you to report the situation so that we can compensate for the failure of the interferon receptors with an antibody treatment. This is now very advanced and has already begun in the USA and also in Germany as the first country in the EU. Our experience, especially with Eli Lilly, has been very positive. However, only if it is started early enough.

Premium clients who have fully active interferon receptors do not require additional treatment at this stage, as their own timely and comprehensive antibody production should kick in. Our C19 Immunization Program has been designed to optimize the T-helper, T-memory and NK cells, and we can therefore assume that the client's own antibody production is sufficient to ward off the worst of the disease.

If antibody production does not start automatically, the virus will have access by means of its spike protein and be able to proliferate. At the same time, if the immune response is weak, the spread of the virus will ultimately be unstoppable. This would become apparent from the symptoms. At this point, the fight against the

virus has been lost. Subsequent treatment in hospital is not against the virus, which has already taken hold, but against the consequences of the virus. The outcome at this point is unpredictable. The real battle begins as soon as the virus enters the system, and this is when intervention is vital.

The recent mutations are known to be much more transmissible, in particular the B.1.1.7 variant, which has almost three times the viral load of the 501Y.V2 variant. This is why those first hours of infection are crucial.

There is a need for a coordinated response at a global level. We are, however, pessimistic as to whether it can be achieved, because neither the WHO nor any other organization is capable of doing so. Nonetheless, this is essential if the pandemic is to be mastered.

We would remind clients that they can keep themselves up to date on the latest developments by checking our Salvagene Premium App at regular intervals. We are uploading the news in ticker form, and in addition to the daily reports and podcasts, we also make individual recommendations, some of which are updated on a daily basis. We recommend that our Premium clients download the app which has been designed for their exclusive use.

SALVAGENE HQ
Université Paris Sorbonne
125 Rue Saint-Jacques, 75005 Paris

SALVAGENE UK
52 Grosvenor Gardens • SW1W 0AU London UF
Tel: 0044 20 3287 0644

SALVAGENE USA
101 Avenue of the Americas, 8th floor • 10013 New York
Tel: +1 646 583 0370

info@salvagene.com • www.salvagene.com