Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #76

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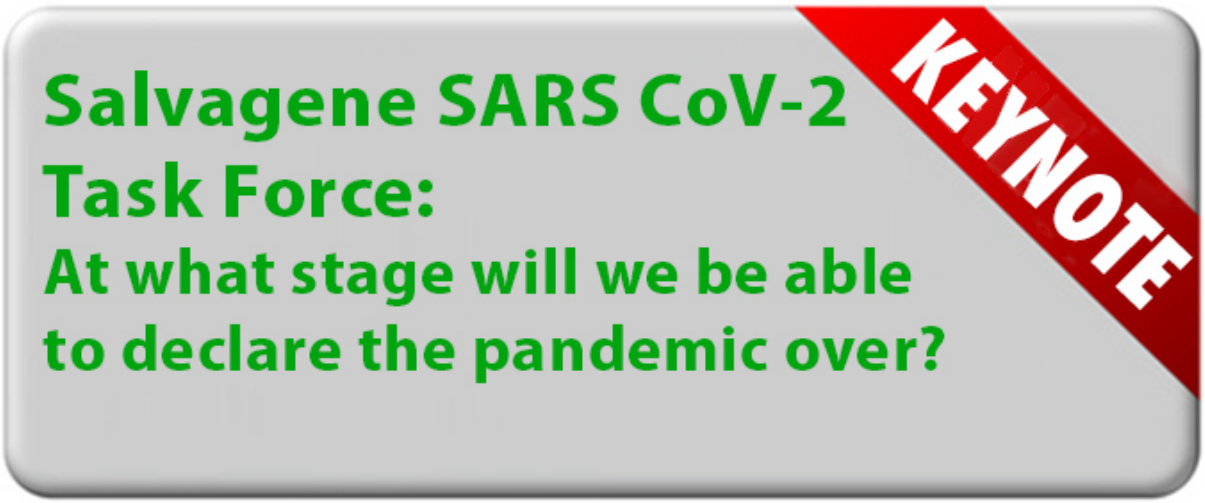

Dear Premium Customers,

We consider it highly improbable that the SARS-CoV-2 virus will disappear from the human species as a result of immunity built up from survived infections and/or vaccination.

We envisage two possible scenarios of how the situation might develop further. In the more favorable case, a mutation prevails that is more infectious but at the same time less harmful than the so-called "wild" type and, most importantly, than the variants we have been reporting on for the past twelve months. The other variants become displaced, so that SARS-CoV-2 ends up being classed along with seasonal flu and the common cold. This would indeed be the absolute best-case scenario. We think it is possible, but not very likely.

Thanks to the much more systematic use of sequencing, which is fortunately now being applied much more widely around the world, it has become clear that escape mutations are more likely to arise among the vaccinated population than among non-vaccinated

people (unless they are on a specific immunological medication). For this reason, it is essential that the vaccinated also continue to be tested, because they constitute the main pool for future escape mutations, and testing is the only way that these can be detected.

Surprisingly, there is only one study anywhere in the world so far that is keeping count of infections passed on by vaccinated individuals. It is a multicenter analysis from Scotland that we keep coming back to, because it is the only one of its kind in the field. The findings suggest that vaccination of medical staff (with BioNTech and not with AstraZeneca) has caused the probability of infection for their family members to drop by just 30%. Even if we were to remove the general risk of infection the equation, this brings the probability of a vaccinated individual infecting a family member down to 50%. An impenetrable wall against the pandemic looks very different from this. The statistics have been compiled from a base of 144,000 doctors and nurses and 194,000 people sharing accommodation with these frontline medical workers, so it is a comparatively broad study.

This leads us to the second scenario in which mutants appear that are not only more infectious but also more dangerous than those known to us so far. The mRNA-based vaccines do, of course, offer a platform whereby they can be adapted to the prevailing conditions at relatively short notice. But the problem here, as we see it, is that this type of vaccine is not globally applicable, firstly because of the expense and secondly because of the technology. Even mRNA vaccines are only ever adapted in critical response mode, and we consider that the right strategy is not being pursued here, namely to respond to mutations, especially with the danger of a super mutant appearing (see previous Keynote #75).

We think a completely different approach is called for. Some of the vaccine manufacturers' research teams are going much further by trying to predict the direction in which mutation events are heading. This is a challenge that can only be met with AI (Artificial Intelligence) and "big number crunching". We are right behind this

strategy, because our own programs are also AI driven. The Salvagene Premium Program is now 70% derived from artificial intelligence, and everything we develop for our customers on the basis of AI brings very significant benefits, for example in the context of cancer prevention. The new projects are also going down this route, and the aim is to bring a vaccine to market by the end of this year at the latest in order to catch the mutations of the virus that will develop in 2022 and to prevent them from spreading in the first place.

The increased application of AI is a modern development that is completely changing medicine as a whole, because without it, key aspects would no longer be manageable. In the formulation of future vaccines, the past 18 months of the pandemic have obviously delivered useful data on which to build AI programs. Now is the right moment for this. The project underway at the University of Austin deserves a special mention, but also the work being done by CureVac in Germany, which we have referenced on several occasions. We are convinced that, if the pandemic is ever to be halted completely, then it will only be as a result of science adopting this approach.

Furthermore, we note with satisfaction that the initially selfish tendencies in the development, production and distribution of the vaccines have been moderated to some extent; on the whole, these tendencies have intensified and are ultimately the core problem of the pandemic. This is because, in contrast to the empirical data established during clinical phase 3, the vaccines do not reflect the reality on the ground. In our antibody profile monitoring, we have reached completely different conclusions about the extent to which vaccination actually leads to Covid immunity. The numbers are much lower compared to the data obtained in the empirical phase 3 clinical trials with their relatively short observation periods and, of course, with very few mutations at that early stage. We do not consider any of the present vaccines to come even close to 70% efficacy.

With the vector-based and protein-based vaccines, efficacy is even lower. The Chinese vaccines in particular have clearly had less success, outside and even inside China, and the same goes for the Russian vaccine, the results from which have been lacking in transparency. All of this has led to more and more vaccine manufacturers banding together across national borders, working on joint projects and sharing their findings, especially in the transition to the next generation of vaccines. Ultimately, this spirit of cooperation has not been adequately supported by governments. Rather, it is initiatives of private companies and university departments – an endeavor that is deserving of praise.

The Com-CoV study at Oxford, which is investigating the efficacy and the side-effects of different vaccine combinations, will present its final results in approximately 1 - 2 months. Against this background, we are highly skeptical of a parallel study conducted by the government in Madrid, which found that a first dose of AstraZeneca followed up by a second vaccination with BioNTech did not cause any further side-effects in the 300 volunteers tested. This is simply wrong. The Com-CoV study in particular shows that there are quite noticeable side-effects. We have yet to be convinced of the benefit to be derived from mixing vaccines. For a start, it is not necessary and makes no sense, even though all vaccine mechanisms work on the same spike protein. Consequently, it is unlikely that mixing and matching is going to enhance the effect.

Furthermore, variant B1.672.2 – the so-called Indian variant – remains an open book. We have deliberately qualified it as "so-called" here, because the Indian government is making strong representations against the use of the term, which is understandable. So far, it is actually not entirely clear how this variant operates, although Public Health England has gone on record to say that both the mRNA vaccine from BioNTech and that of AstraZeneca have good rates of efficacy against this specific variant – 88% and 60% respectively. We are always amazed at how quickly such results are published. In order to test efficacy long-term – and not only empirically but also clinically – it takes

weeks or months. We are therefore extremely cautious about accepting such claims. That there is a high efficacy rate against the Indian variant is undisputed, but we cannot endorse this way of calculating vaccine efficacy, not least because of our experience in the past. Just how real is the immunity obtained from vaccination when compared with our Antibody Immunization Monitoring?

In most of the variants we examine closely, we keep finding the same mutation, namely E48.4K, which has even now appeared in a French variant. We are therefore dealing with the same or similar mutations on a spike protein, and it is possible that the pressure on vaccine developers to adapt their product will not be so great in future.

None of the vaccines developed so far – not even the mRNAs – are without problems. So, for example, the Centers for Disease Control and Prevention (CDC) is now recommending an investigation into cases of myocarditis (heart muscle inflammation) that have occurred subsequent to mRNA vaccination. With the vector-based vaccines, a thrombosis can be triggered by predisposition and the various risk factors (e.g. the Factor 5 Leiden gene) that are innate to a person. Similarly, there are several genetic polymorphisms involved in myocarditis; these form part of our standard checks for Salvagene Premium clients. We should also note an indirect effect on inflammation of a certain polymorphism on the QT interval. In theory, we are therefore able to test processes to determine which type of vaccine is the optimal one for the individual client. And that is exactly what we set out to achieve: advice on choice of vaccine is given on an individual basis, because there are many variables to consider. Vaccines work in very different ways, and there are too many different versions and boosters. The need for personalized recommendations keeps growing, and it becomes more and more complex with every major mutation event and the frequency with which an individual has already been vaccinated. All of these factors have to be constantly monitored and collated.

We can see exactly what kind of side-effects result in both the medium and the long term. The package insert that comes with a vaccine cannot tell us that. The primary changes that the organism immediately displays are epigenetic in nature, especially at the inflammatory and cytokine receptors which we include in our Covid-19 Immunization Protocol in order to gauge what kind of side-effects the vaccines are producing. This is all based on the assumption that there are positive side-effects that trigger certain stimuli. But, of course, there can also be negative consequences. At the end of the day, any scientist is essentially peering into a crystal bowl in trying foresee what sort of effects vaccines will have in the future, and that is why we include these effects in our program. For example, several of our Premium clients were injected with the Johnson & Johnson vaccine and no antibodies were subsequently detected in their samples. Consequently, the vaccine had failed to achieve its purpose of immunizing those clients.

The question of when the pandemic will end can also be considered from the perspective of epidemiology, in which the concept of the "social end" is defined. It means that the pandemic does not end when the danger to health has gone away, because we can reasonably assume that this will never disappear, but rather when the population is no longer subject to general restrictive measures, feels confident enough to ignore the dangers and, as a result, is once again willing to accept the increased risk of hospitalizations and/or death, as was the case with the Spanish flu. This is the social end of the pandemic, which is already becoming visible in parts of North America and Europe.

It is somewhat surprising that these are the very regions of the world where a sentiment is already perceptible that the pandemic is approaching its end. From a global perspective, however, it has to be acknowledged that the fight against the virus has only just begun. In Europe, you may think that you can see the light at the end of the tunnel, but if you are in Nepal or India today, that prospect seems a long way off.

Modern societies are simply more mobile than flocks of sheep, and the mutations that take place in other parts of the world will continue to undermine the best efforts to achieve global immunity. Developments between autumn and next spring will give us a clearer idea of the direction in which the pandemic is headed.

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