Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #68

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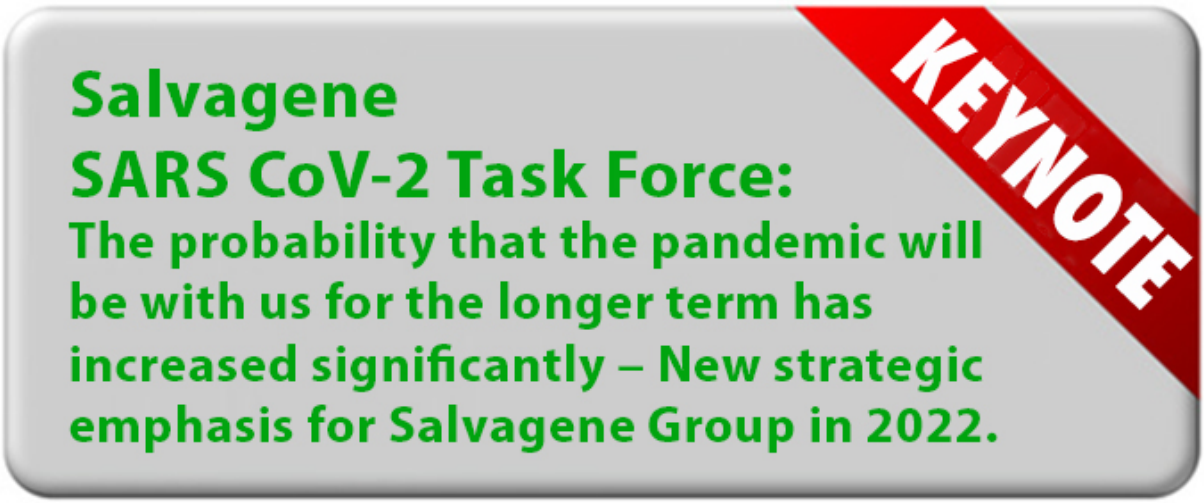

Dear Premium Customers,

We consider that the likelihood of a major vaccine campaign bringing the pandemic to an end this summer is diminishing. With this long-term scenario in prospect, we at the Salvagene Group have had a strategic rethink, not least because we have been allocating so much of our resources to SARS-CoV-2 research over the past twelve months. We now intend to significantly expand capacity in our core expertise, namely cancer prevention, to avoid a situation where this priority is repeatedly pushed to one side. We have to work on the assumption that the SARS-CoV-2 virus will keep us occupied for a long time to come. To meet the challenge, we will be reorganizing and significantly expanding our research capacities.

After one year of the pandemic, it is clear that years of effort on our part aimed at optimizing the health of our clients so that they are better able to withstand infections – with or without the benefit of vaccination – can be undone in just a few weeks. The risk posed by the pandemic is as at least as important as all other non-related health maintenance issues. There are several reasons why we have raised the alert level, in particular the notable increase in mutation events over the past 14 days. The fact that infection rates have continues to climb as the various vaccines are rolled out shows that immunity to inoculation is being created by the escape mutations. The world is currently in danger of having to start the entire vaccine campaign all over again.

We consider one of the main reasons for the sharp increase in mutations is the deployment of vaccines with limited efficacy, especially against the new mutants, and the policy of delaying the second jab. This is not entirely unexpected. Our dealings with the vaccine manufacturers, with WHO officials and with government agencies have confirmed us in this view. Almost all vaccine manufacturers are already working on the third generation of vaccines. What has become quite apparent is that vector-based vaccines are at a considerable disadvantage, and in some cases, the platforms are having to be completely redesigned. We forecast that future vaccines will have almost nothing in common with the original Wuhan variant.

As we wrote in a previous Keynote, regulatory authorities around the world will turn a blind eye to this and are already signaling that they will not demand a new approval procedure, even if the vaccine has only limited similarities with the original platform. As we predicted, the less than 100% efficacy of all vaccines currently being administered is being further reduced by the latest mutants. If normal WHO licensing guidelines were followed and the mutants were the predominant variants, none of the currently licensed vaccines would be granted approval.

Oxford University has published excerpts from a study of AstraZeneca vaccine in South Africa. However, we have had sight of the entire study. It shows that the vaccine produces nine times fewer antibodies against the South African variant than the original Wuhan virus. As we mentioned in Keynote #67, we believe that too much emphasis is placed on the total quantity of antibodies. With our new SARS-CoV-2 antibody profile monitoring, we have much more detailed ways of finding out how effective antibody production is in an infection and/or vaccination. From the same study, it is clear that vaccination has also produced antibody-dependent enhancement (ADE), which is very bad news indeed.

This is one of the main reasons why we have recommended that our Premium clients with top immune response results delay vaccination for the time being, as we see various vaccines going down a blind alley with the way the SARS-CoV-2 virus is developing. The old adage holds true, that the manufacturer who is first to market is not always the winner. Even BioNTech is experiencing significant problems in terms of efficacy against the new mutants.

We are currently investigating several cases where AstraZeneca has been administered within the intervals laid down by the manufacturer yet where infection has occurred within a very short period of time. Comparing antibody profiles immediately after vaccination with those immediately after infection, it is becoming increasingly clear that what applies for this version of the vaccine also applies to a lesser extent for all the other vaccines that are currently approved. The advantage of newer vaccines such as Novavax and especially Curevac, which is also mRNA-based, is that they have been developed against a background of the current mutation events.

We have information relating to one of our own Premium clients in New York who became infected relatively soon after receiving the second of the two BioNTech jabs. We are also aware of several individuals who had received the Moderna vaccine, so it can be seen that all currently available vaccines are affected. The project to observe the different infection incidences in the different states of the USA is highly interesting for us. In particular, the variant B.1.526 and the variant B.1.525, which were discovered in New York at the end of last year, have been given a significantly different classification by us than that applied by the Centers for Disease Control and Prevention (CDC). We surmise that the current vaccines have a clearly reduced effect. This could be one of the reasons why the incidence of infection varies greatly between New York and, for example, Florida. Other reasons could be the different climatic conditions, etc. The same applies to California with the variants B.1.427 and B.1.429, which we consider to be much riskier than the CDC does. Hence, it is essential to observe infection incidence in connection with vaccination.

Consequently, **there is no alternative to optimizing our own immune response as much as possible. Once again, we ask our Premium clients to adhere to the C-19 Immunization Program as strictly as they can, because this is still by far the best protection.** None of the vaccines available so far offer anywhere near the effectiveness of a balanced and complex immune response, as almost all vaccines focus on antibody production.

The viral load is much higher with the new variants – up to twenty times higher with P1 – and the aerosols are much more dangerous and take much longer to break down indoors. Unfortunately, this is not a matter of hours or days, because an aerosol created by an infected person with high viral load can persist for well over a week and infect someone who enters the indoor space many days later. So, again, we would refer you to the updates in our C-19 Immunization Program which has increased relevance whether you are spending time outside or inside.

We also need to say something here about children and adolescents, because they are clearly more at risk from the new variants and also play a greater role as virus carriers. The long-term effects in young people are in any case becoming more visible, manifesting themselves as fatigue and pain. One additional factor here, of course, is lockdown and its mental and physical toll. We are monitoring all relevant projects, as the vaccine manufacturers seem to offer no answers at the moment. We see with Johnson & Johnson at least that they are the furthest along, so for teenagers we would most likely recommend the Pfizer or Johnson & Johnson vaccine. So far, none have been approved for this age range, but we will inform you as soon as they are.

After several weeks and months of administering millions of doses worldwide, the side-effects of vaccination are becoming more visible. And it is still true that the vector-based vaccines are producing considerably more side-effects of a short-term nature – by which we mean weeks and months – than the mRNA-based alternatives. In terms of side-effects, however, the latter remain more of an unknown quantity for us in the long term.

In Europe, the issue of sinus vein thrombosis with fatal consequences is a major worry. This does not concern AstraZeneca alone, because all vaccines can trigger thrombotic events. Even though the EMA has reaffirmed its approval of the AstraZeneca vaccine (with the proviso of information on side-effects being included), we have our reservations. AstraZeneca has advantages and disadvantages, but the way in which the EMA has approved it comes as a disappointment to us. This is because the EMA is one of the very few regulatory authorities in the world that has a limited, proper approval procedure, while the vast majority of bodies in other parts of the world deliver emergency approvals, and the manufacturers are thus more or less completely absolved from liability.

One thing that the EMA should have done is lift the age restriction, because this only came about because AstraZeneca's published clinical phase 3 data included relatively few participants in the older age group, which left everyone guessing. Much more data has since been compiled, and AstraZeneca can now be recommended for older people. Especially because a proper immune response definitely needs to produce T-helper cells in addition to and perhaps even more urgently than antibodies. And new T-helper cells need to be produced so that the immune response is accurate and not so diffuse as to compromise its effectiveness. This particularly affects older people, because they have already acquired many T-helper cells in the course of their lives, but obviously these were not produced specifically to target SARS-CoV-2. In theory, they need a boost to their T-helper cells. This is where AstraZeneca's great strength lies. As mentioned earlier, we recommend this vaccine for older people if none of the other vaccines on our list is available.

The situation is completely different for young women, and we have seen several cases of sinus vein thrombosis among this group. Some countries have continued to inject AstraZeneca without restriction. In others, including Denmark and Norway, the vaccine remains on hold. On Monday, Canada suspended the use of AstraZeneca vaccine for people under 55 years of age, and in the very latest development, all of the Berlin hospitals, including the Charité, have cancelled vaccine appointments for women under the age of 55 in response to a cluster of thrombosis cases. The Standing Commission on Vaccination (STIKO), which advises the German government, has just recommended that the AstraZeneca vaccine should only be given to people over the age of 60.

We think it is right to refrain from injecting it into younger women who have a certain polymorphism in the wild-type factor 5 Leiden gene. We are highly skeptical about the use of certain hormonal contraceptive methods anyway where this variant is present. We believe that the taking of certain hormonal contraceptives by

women with this gene variant coupled with the administration of the AstraZeneca vaccine may be the main reason for the sharp increase in cases of sinus vein thrombosis. These are of course small in relation to the total vaccinated population, but pose an existential risk to the individual concerned. Great efforts are being made to get the AstraZeneca vaccine approved in the USA, but they are meeting with resistance from the NIAID health authority who have requested more data and further interim analyses. We see sinus vein thrombosis as a general problem for all vector-based vaccines, albeit to varying degrees.

In summary, we feel vindicated in our assertion that there is not and never will be the perfect vaccine that works for everyone equally, in terms of either effectiveness or side-effect risk profile. It is therefore important that a vaccine is selected individually for each recipient. The same goes for the administration of booster jabs. As with any medicine, of course, recommendations on the choice and timing of a vaccine and/or booster are specific to age, gender and the individual's health factors, because any study will only ever show a statistical mean or average.

Since we set up our Salvagene SARS-CoV-2 Task Force about 15 months ago, one of the key questions that keeps cropping up and has significance in determining the further course of the pandemic is how the virus came about in the first place. We have had an open mind as regards the two main theories circulating, namely was it by transmission from animals (possibly bats) to humans or was it a laboratory accident? The official statements emanating from various government agencies and the WHO favor the animal-to-human transmission version, which would obviously be bad news in terms of future mutations. We estimate the accuracy of this animal-to-human transmission theory to be lower than before – somewhere around a 50% probability. There is growing evidence that there have been no reverse transmissions from animals so far. Even though we may be going against the mainstream, our team is coming around to the view that a laboratory accident may have

been the trigger. The one positive to be drawn from this theory is that reverse transmission between animals and humans would, in the long run, make it much more difficult to ever get the pandemic under control. So perhaps the wish is father to the thought.

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