Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #46

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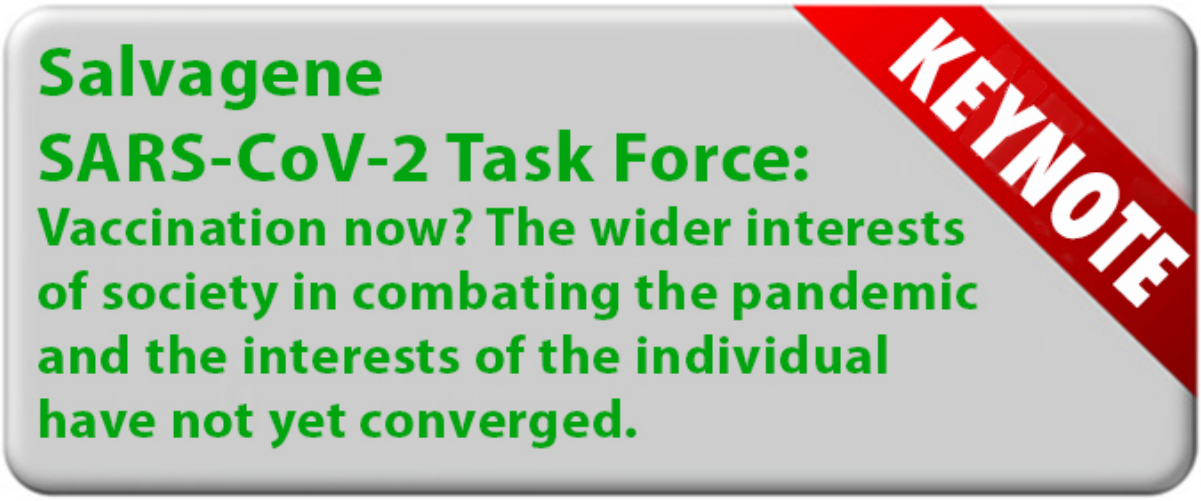

Dear Premium Customers,

What is best for society in its efforts to control the pandemic may not necessarily coincide with what is best for the individual.

In recent days, our Salvagene Vaccination and Medication Advisory Board has been communicating its preliminary recommendations to clients on whether they should get themselves vaccinated. The clients who have been contacted so far have without exception been those who have a Covid-19 Risk Factor higher than 2.8 and Cytokine Storm Risk Factor higher than 2.5. But even in this high-risk group, we have not yet made any firm recommendations. This is not only because of the potential risks of vaccination, but also because of the multiple problems faced by any vaccination campaign in December and January. We have taken a close look at the current situation in all OECD member states regarding infrastructure, availability of the different vaccines in the next 8-10 weeks and respective national vaccination strategy to the extent that one has been mapped out.

As we reported in a previous Keynote, the country with the most advanced vaccination strategy at present is the UK. And this is

where we are already seeing the first problems. We see this as a testing ground which will show up any potential difficulties along the way. The first of these is that the 5 million doses ordered for December have now been reduced to 700,000 usable doses by the Joint Committee on Vaccination and Immunisation (JCVI). This is mainly due to quality problems with the doses of vaccine already produced, as we have already reported. Last Thursday evening, the first batch arrived in the UK from the Pfizer factory in Belgium for distribution to around 50 hospitals. Here too, the NHS has demonstrated its strength in terms of logistics.

We think that the USA will be first among the OECD group of states to follow the UK in having its own emergency approval, at least for the Moderna vaccine. They will then be followed by the European Medicines Agency with a significant delay of at least 3-4 weeks. The EMA has already stated explicitly that it wants to take more time than the other authorities, especially as the clinical data from the trials is still not available.

The EMA will make a decision on the BioNTech vaccine on 29th December, and a few days later the EU Commission will give its official approval. The UK government has only issued an emergency approval, whereas the EU will give a conditional marketing authorization, requiring compliance with much stricter regulation than for a fully authorized product. An emergency approval, on the other hand, gives permission to temporarily use a product that has not yet been officially authorized.

Our Advisory Board on Vaccines has been hard at work for several months now, and we have been closely monitoring the top projects. We therefore believe that we are in possession of more information than has so far been published, although it has to be said that we do not have detailed results from the clinical trials of all projects, as these have not been published. So it is still completely unclear what age groups were involved and what adverse effects if any were detected in the individual populations. It is also completely unclear how long immunity lasts and

whether a booster jab is required. Although there has been no evidence of a multiplicity of severe, acute side-effects, this does not necessarily mean that the vaccine is safe and that there is no need to worry, as some high-ranking officials in various countries have gone on record as suggesting.

And herein lies the problem. To control the pandemic, it obviously makes sense to roll out a program of vaccination as soon as possible, and it is of course a stroke of luck that we now have working vaccines. On the other hand, the risks for the individual are still enormous. Also, we have no information as to whether any especially vulnerable individuals were included in the trials, as this group tops the priority list for a national vaccine strategy. Almost all countries have drawn up more or less the same categories of priority. And, of course, the possible long-term side effects remain unknowable. This applies in particular to the mRNA-based projects, which we acknowledge may cause epigenetic changes with unforeseeable collateral damage.

In the absence of data from the clinical trials and without the customary level of transparency, it is very difficult for any consultant or physician to offer advice, in particular to high-risk patients. It goes without saying that this is an exceptional situation, which makes things a lot more difficult for a large number of colleagues who may be privy to far less information than Salvagene and can therefore only try to give advice based on press releases from the manufacturers. It is a true dilemma.

What is officially available are the interim analyses from Phase 2, but the decisive factor is of course the data from Phase 3, namely the randomized clinical trials on safety and efficacy as compared with the control group. What’s more, the efficacy rates of 90%, 94% and 95% given in press releases together with caveats and the muddled results from the AstraZeneca trials show that the rushed nature of these projects is bound to throw up further problems.

It would be of particular interest to be told who was tested, which endpoints were set, what was the percentage of elderly people with underlying conditions, and whether there were any high-risk patients among them. This information is completely missing.

As we have pointed out with particular reference to the Moderna vaccine, the efficacy rate is derived from relatively small numbers. For example, BioNTech quotes a figure of 170 infected persons, 162 of them in the control group and 8 in the vaccinated group. In the case of Moderna, the figure is a mere 90 vs. 5 which, in our view, represents only a limited number of events. What the results do not tell us is who these 170 or 95 infected people were. Were they younger people who tested positive but without symptoms? Or were they older patients who fell seriously ill? We are also interested in individuals whose immune system is so impaired by underlying conditions that they do not produce antibodies at all. Were such individuals also part of the trials?

Admittedly, the accelerated approval procedure – the so-called "rolling review" – makes perfect sense from the angle of combating the pandemic. As we see it, however, some of the steps that have been skipped are by no means minor. For example, human trials were started even before the tests on monkeys were completed and fully evaluated. Our colleagues at Science Journal have also commented on this.

We think there is minimal risk, although we cannot rule out with certainty the possibility, that the mRNA vaccines might be carcinogenic. We are working on the assumption, based on our own specialist knowledge, that the cancer risk is not significantly increased.

We believe that there is a difference between pandemic management on the one hand and the choice that the individual makes for or against vaccination. Both depend on an as yet unclear aspect of mass vaccination, because this can only be effective if the vaccines give so-called "sterile immunity", which means that the risk of a vaccinated person passing on the virus is excluded. We await enlightenment in this regard. The regulatory

authorities, in particular the EMA, are insisting that the volunteers from the trials are monitored over the long term, not only to detect any late side-effects, but also to gauge how long the immunity lasts and whether sterile immunity occurs.

With regard to safety, it is important in the case of older patients who fall ill or even die after a Covid-19 vaccination to establish whether the vaccine is to blame or the underlying disease. How is this aspect to be managed? The SARS-CoV-2 Salvagene task force is currently drawing up a proposal for a directive.

So, before making any further recommendations to Salvagene clients with Covid-19 and Cytokine Storm Risk factors in the lower range, and despite our privileged knowledge of the vaccine projects, we have decided to wait at least until the full clinical trials of the three, four or five lead contenders have been published, and we expect this to be done sometime between the second and fourth weeks of January. Your Salvagene consultant will then contact you directly.

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