health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

Ministerial Advisory Committee on Vaccines – Meeting with Gamaleya

Date: 30 March 2021

Time: 10:00 – 11:30

Venue: Zoom Link

Meeting Minutes

Attendees:

Prof Barry Schoub (BS - Chairperson); Prof Helen Rees; Dr Hannelie Meyer; Prof Ames Dhai; Dr Owen Kaluwa; Prof Willem Hanekom; Prof Richard Lessells, Prof Gregory Hussey; Ms Glaudina Loots; Prof Jeffrey Mphahlele; Prof Penny Moore; Dr Alex Sigal; Dr Angelique Coetzee; Dr Morena Makhoana; Prof Rudzani Muloiwa.

Guests:

Dr Daria Egorova, Arsen Kubataev, Nina Kandelaki (Head of Health, RDIF), Alexandra Marchenko, RDIF, Alexey Egorov (Russian Embassy), Elmira Muslimova, Valeriya Zadoro

Apologies: Prof Clive Gray; Prof Wolfgang Preiser; Dr Boitumelo Semete

Secretariat:

Mrs Nasreen Seedat; Ms Khadija Jamaloodien; Dr Ruth Lancaster; Ms Marione Schonfeldt; Dr Lesley Bamford.

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1. Welcome & Apologies

- The Chairperson welcomed all the members to the meeting.
- Members of the VMAC and Gamaleya introduced themselves.
- The main topics of interest was the effectiveness of Sputnik V on 501Y.V2 variant and issues around the Ad5 vector.
- Prof Rees indicated that the VMAC is a scientific, advisory committee to the Minister of Health, regarding the Covid-19 vaccines. Of importance to the South African situation are

data on the variants, particularly the 501Y.V2. Of particular interest as well is how far Gamaleya is with Sputnik Light.

2. Gamaleya

- An article published in Lancet (Feb 2021) on the efficacy of Sputnik V showed 91.6% efficacy. A separate trial in elderly people showed an efficacy of 91.8%. The efficacy against severe cases was reported at 100%.
- The vaccine is based on well known virus platform (Ad26 and Ad5). Gamaleya used this same combination in the MERS and Ebola vaccines, which showed high safety of the vaccine. The mass vaccination in Russia is also showing high safety and immunogenicity. Study results from Mexico are also showing similar results.
- The vaccine is stable at 2-8 °C for 2 months and aiming to have increased stability which is important for country logistics.
- Sputnik V is approved in 57 countries under Emergency Use Authorisation.
- Sputnik Light (single dose of Ad26):
    - First component of the Sputnik V. Registration dossier sent to Russian regulatory authority yesterday (29 March). EUA is expected in 3 weeks.
    - No separate trials have been done for the Sputnik Light within the Phase 3 Sputnik V study. Only Phase 1/2 trial in 110 people has been done and a strong response was seen in 100 patients.
    - Results showed that a single dose of vaccine is capable of producing antibodies in 98% of subjects on day 28 of immunisation.
    - Immunisation of subjects with pre-existing immune response showed a boosted immune response (IgG) in 100% of participants.
    - Neutralising antibodies seen in 95.7% patients on day 28.
    - Efficacy of 1st component within the Phase 3 trial were reviewed, before the 2nd dose was given. This showed a 70+% efficacy (however, note that this is extrapolation from about 7000 patients as the trial was not geared towards measuring the Sputnik Light).
    - Patients are being enrolled in Ghana, and Serbia as well for Sputnik Light.
    - It is believed to be a good vaccine option for younger people and those who have already been exposed to Covid.
- Tested against the British variant (501Y.V1) and still awaiting the report.

- The South African variant (501Y.V2) has just arrived today in Russia for laboratory testing. Gamaleya will have some data in the next 2 to 3 weeks.
- They are also awaiting the variant from Brazil to arrive this week.
- Ad5:
    - HR: Concern with using Ad5 in the South African population because of the high incidence of HIV. Previous work both in the Phambili and the Step studies showed that using Ad5 increased susceptibility to HIV, particularly in uncircumcised males.
    - Dr Egorova: The concerns with Ad5 are based on 2 trials of a vaccine made by Merck for HIV. The vaccine was not successful, and there was a sub-group of patients (male, pre-existing immunity to Ad5) who, several months after vaccination, showed increased risk of contracting HIV. This is the basis of concern of using Ad5 for this subgroup of patients. Gamaleya's position: on one hand there were many trials using various Ad5 vaccines, these trials have not identified any serious risks of increased risk of contracting HIV. These risks were statistically justified. However, this was only a small subgroup and if we think of the overall population, no increased risk was observed. Also, the risk observed in the subgroup of patients was not permanent. One or one and a half years after the prevalence of HIV in these patients was similar in overall prevalence. To note that this trial was for a vaccine against HIV, so it included participants at highest risk due to lifestyle etc. Also, these trials were conducted more than 10 years ago and there is still no scientific explanation for this, which could possibly be a statistical anomaly. Gamaleya is collecting data on patients in Russia receiving the vaccine. This registry also contains all pre-medical history of the patients. There are plans to conduct a detailed analysis of the registry after a year including events to acquiring HIV. Currently however the only source of info is the observation made in 2 trials conducted 10 years ago. Without further studies they are not able to assert those risks unequivocally. Not confident that this is a real risk as there is no scientific explanation for those results.
    - Gamaleya also owns a collection of viruses including the SARS- CoV-2 variants. They are collecting all variants in Russia as part of regular process and checking sera of patients vaccinated with Sputnik. It has been observed that none of the Russian variants have the decreased efficacy of the vaccine.

British variant – no reduction in antibody neutralising effect was seen. As soon as the data on the SA variant is available, it will be published so that it is publicly available.

- In the vectors there is the full sequence of the Coronavirus, the amino acid is the same as the wild strain. They did not follow other manufacturers which used the mutant stabilised version of the virus as no difference in immunogenicity was seen between the variants. It is believed that this difference from other vaccines leads to higher secretion of a larger variety of antibodies and the immune response is more polyclonal which in turn will enable a response to the variant strains and will prevent the risk of the vaccination being non-responsive to variants.

- HR: With regard to the SA variant – would you also review against the Sputnik Light as well as the 2-dose vaccine?
- Dr Egorova – yes, will consider sera from volunteers from Sputnik Light. Also, part of the clinical initiative in Moscow is to receive sera from participants who had Covid, and those who were vaccinated and want to donate plasma. They are accumulating a wide array of data.

Questions and Answers

- Alex Sigal:
  - Introduced himself as being a member of the of the laboratory that sent Russia the 501Y.V2 variant sample. Can we collaborate on the study on the variant?
    Dr Egorova – yes, ok to get together to plan future actions, and will engage with you on when to share the data.
    Alex – Ad5: do you have any idea whether it is a problem or not?
    Dr Egorova – only have a general idea of the problem but as there is no data as yet, it requires a new trial for this.
  - Arsen – Does the Ad5 really require a clinical trial, or are there any lab markers that can access whether the Ad5 from Russia is any different to the one used by Merck? Any ideas on what can be done to get a quicker answer instead of a long and expensive clinical trial?
  - Alex: How to determine whether there is a risk of HIV infection – can use in vitro infection markers, Ad5 vaccine cells and compare data to Ad26. . There is already some data on this HIV samples can be sent to Gamaleya. It would

be easier for SA if we could also confirm your results with the 501Y.V2 variant. It would be easier to process in SA and we would have results from 2 systems from live virus and in vitro virus.

- Dr Egorova – will contact Alex to discuss more in detail on what can be arranged as a collaboration.

- Richard Lessells:
  - Efficacy of main phase 3 trial – was the Lancet paper just an interim analysis? Can you share updated efficacy results?
  - Dr Egorova : we will release updated information on efficacy when the participants reach the 6 months of observation period as per the protocol, which will be about June 2021. In addition, there is a registry on the real clinical practice of using this vaccine. It includes data on prevalence and can use data from this registry to see prevalence in overall Russia compared to the clinical trial.
  - SA variant – if there is access to all samples in Russia, there were some 501Y.V2 variant observed in Russia in January, do you have access to these samples?
  - Dr Egorova: We had to wait for the virus to arrive from SA, as we didn't have access to the cases discovered in Russia. The Epidemiological Surveillance Body in Russia identified this variant in the travellers, but Gamaleya did not receive the material in time to isolate the variant.
- Helen Rees: Roll-out data:
  - Are you seeing high efficacy against severe disease and hospitalisation?
  - Dr Egorova: Interim analysis observed that amongst 78 cases, there was no severe or moderately severe cases registered. To date, we cannot make comparisons of subgroups of patients as there is nothing to compare with.
  - Are you seeing consistency in older people in the rollout data?
  - Dr Egorova: Still awaiting data. An immunogenicity study is being done in > 60 year old patients. Seroconversion rate of virus neutralising antibodies is no different to patients >60 years and younger (30-40 year old) patients. Slightly higher efficacy of vaccine in youngest patients (18-25yrs).
- Barry Schoub:
  - What is the neutralising potential of vaccine sera against 50Y.V2 variant? Can you provide panels of sera to provide neutralisation tests in SA as well?

- Dr Egorova – The plan is to do this in the upcoming weeks. Once the SA variant is received, we will schedule a meeting with Alex on way forward. Afterwards we will start the virus neutralising study. This will take some weeks.
- Arsen – there are some regulatory restrictions to send sera to SA, and it was easier to obtain virus and bring into Russia.
- Insert for the vaccine – is this from the Wuhan or the later 614g? is it the full-length protein gene?
- Dr Egorova – we used the nuclear sequence from Wuhan strain as this project started early.

- Penny Moore:
  - Have you been able to share sera from your trials with any other labs?
  - Dr Egorova: There are regulatory restrictions inhibiting sharing sera with other laboratories, as per the informed consent of the trial. RDIF is trying to look into this from legal point of view if it is possible to share.
  - We have been approached by a local SA lab (Dr Reddy's), who wants to distribute the Sputnik V and has asked the lab to test the samples.
  - Nina: We have not yet found a way to export sera outside the country. We are still looking into this and would like to share with Italia Scientific Institution as well. We are investigating whether any exceptions will be allowed. We are not aware of any agreements with any SA lab to ship the sera. Partners from India (Dr Reddy's) cannot ship sera out of India either, hence they want to make their own trials with their own variants. India only has 30 samples.
- Helen Rees:
  - This pandemic is showing the importance of sharing samples so the ongoing discussion on sharing samples is important.
- Jeffrey Mphahlele:
  - Sputnik V is the earliest vaccine to be given to the public. Is there any data on the durability of the immune response (antibodies and T-cells)?
  - Dr Egorova: We are collecting data on all vaccinated persons as part of real clinical practice. This is a complicated process, as there are no mass screenings of antibody titres after vaccination. However, we do have people being vaccinated as part of clinical practice who are interested in their titre of antibodies and have started investigating this. They have however used different scales and units, so it is difficult to compare. Although we are unable

to give data on this from vaccination, however, the seroconversion rate is higher than 95%. Also, in other countries people vaccinated looked at their antibody titres have collated in initiative groups and various communities and posted on social media. In 1 and a half months after vaccination the neutralising antibody titre decreases slightly but is retained for at least 6 months. Cellular immune response is a complicated test and depends on how much time passed after vaccination in order to determine T-cell immunity. There is only a small pool of this data from civil vaccinations. Overall, this responds to clinical trial data.

- Rudzani Muloiwa:
    - Do you have any data pertaining to vaccine efficacy impacting on transmission?
    - Dr Egorova: Unfortunately, there is no data on this. We are trying to work on this at the moment and this data will most likely come out after the data from the trial has been analysed. It has been identified that there are people who are super spreaders, as well as those that also don't transmit when infected.
- Helen Rees: any last questions and comments from Gamaleya:
    - Dr Egorova – thanked the team for this discussion.
    - Nina – RDIF is looking forward to collaboration with SA on the vaccine.
    - Arsen – There is a need to look at the benefit-risk ratio, especially with regards to the Ad5 component of the vaccine. With regards to the HIV trial, it was reasonable to stop the trials, however, with Sputnik V there are benefits to the larger population and the risks are only to a small subset of population. Would Sputnik Light be considered for registration given all the Ad5 questions?
    - HR: The ongoing discussion between Alex and Daria regarding what can be done in the lab is important. Also, the difference between this Ad5 and the Merck one is important. On a personal note (which hasn't been discussed with the VMAC), there may be importance to look at different scheduling with different populations e.g., a single dose in younger people. This virus will be with us for some time, and it is thought that this might be a continually mutating virus that may need annual vaccination like with flu virus. The 501Y.V2 is not only a SA problem, as it is emerging in other countries. Therefore, any collaboration between the SA labs and your labs is incredibly important. It is recommended, if possible, for Gamaleya to export sera to SA labs so that

consistency between the lab assays can be measured. In addition if Penny/Alex can follow up on looking at the Ad5 question. We will be very interested in your June data and the data from sputnik light.

- BS: the point about risk:benefit is a good question, and we will need to look closely at the Ad26 Sputnik Light regimen. For certain groups possibly higher risk (elderly, women, etc. who are not at potential risk from the Ad4) may well benefit from the Ad5 booster. But the VMAC will be looking into this.

Meeting with Gamaleya concluded at 11:31.

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3. VMAC Debrief

- HR: This was a good discussion with extensive background given. When looking at the Sputnik V, it has high efficacy and neutralisation titres, however, the impact against the SA variant needs to be looked at. The Ad5 is a difficult unanswered question as more data would be required which could be included into the rollout. The Sputnik Light is of interest and Willem has shared data that suggests that this is a highly effective vaccine depending on how it behaves in terms of the variant. Programmatically, having different vaccines for different populations may be problematic.
- PM: There is frustration that Gamaleya is slow to generate data against the variants. Even if there are regulatory hurdles, there should be other labs in Russia running assays on the pseudo typing level. They should be pushed to send sera here. Regarding the Ad5, it is uncertain how easy it will be to set up a lab proxy for that, but further discussions can be held.
- AS: There would be a lot more trust in the vaccine if the sera could be tested in SA. For the Ad5 there is no easy answer and perhaps in vitro T-cell infectivity can be a proxy. The first priority, however, should be to check the variants and see how neutralisation works as there is growing consensus that is associated with protection. It may be also worth looking at what the effect is on HIV infection.
- HR: From the interim analysis, the vaccine is clinically effective, which seems to be reinforced by the population rollout data. It seems like in the data that has been looked at with correlates, it was the relative titre and if this is coupled with clinical data it is very good.

- WH: Confirmation of correlates of protection will be available in a month or two but it is likely to be an antibody response of some sort. For now, the clinical results must be looked at and the biggest concern here is the Ad5 issue, including the full version versus the light version. Within the South African setting, it is an extraordinary risk, and there is uncertainty at this point how to address this issue. Recommended to involve Linda-Gail Bekker and Glenda Gray in this discussion.
- HR: Alex, Penny and Richard to have a side discussion on the Ad5 issue and look at how data can be generated experimentally.
- JM: Is there a minimum set of laboratory experiments and data that can be done to answer the issue of the variant so that the different vaccines can be assessed for suitability (in the absence of clinical data)?
- AD: It was heard through the media that the President has secured 30 million J&J vaccines to be purchased soon. Considering this, what is the reason for meeting with other manufacturers? Is it due to the durability of the J&J vaccine being unknown, the uncertainty with the Pfizer contracts or understanding of boosting with different vaccines going forward?
- HR: At this stage, it is wise not to put all your eggs in one basket, not only from a scientific durability point of view but the manufacturing challenges as well. The second point is it is important to look at different vaccine technologies as some are easier to adapt to the variants than others. The third point is the cost as it was seen with the AZ vaccine that we were being charged twice as much as the EU. We also have to be careful as an advisory group to have a level playing field and scientifically its advantageous to know what is out there. In addition, South Africa has driven the research on variants as a global agenda which is crucial.
- BS: As the MAC we must have a strong advisory that we cannot be dependant on a single vaccine manufacturer. There is an appeal to the laboratory expertise to look at the Sputnik V vaccine as it has many procurement advantages. Scientifically we need to be satisfied with the efficacy against the variant and the Ad5 issue as well.
    - How does the Sputnik Light compare with the J&J vaccines as both are Ad26? Are there differences in the vectors or is there a different insert?
    - Is a reduction in neutralization of antibodies an important signal to be looking at or would this be disregarded completely?
- PM: There is a suite of immunological measurements to address JM's point. The issue is that the correlate of protection is still unknown, and we are cautious in reading too

much into the assays without a clear correlate or protection. The magnitude of the loss of neutralisation is similar across the assays (with the different vaccines). Once the correlate of protection is known, interpretation of these assays can be done properly.

- AS: The assay work should be continued as there is an association that can be seen with low levels and poor vaccine efficacy. This data will be important to support the other data that will be coming. In terms of the work done by this group, this is a global disease and there will be a lot of vaccines in Africa for various reasons and it is beneficial to engage with as many people as possible to gather data and establish a base at which the different vaccines can be compared against the variants.
- HR: At the next meeting, the data that is emerging with correlates of protection can be looked at and how to interpret this.

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4. Closure

- All attendees were thanked for their participation and presence.
- Meeting Closed at 12:05.