Minutes of the extraordinary NERVTAG COVID-19 meeting on SARS CoV-2 variant B.1.1.529

Date & Location: 15:00 – 16:00, 25 November 2021 - Via telecon only
In attendance: Chair: Peter Horby (PH) NERVTAG Members: John Edmunds (JE), Wendy Barclay (WB), Julian Hiscox (JHi), Ravi Gupta (RG), NERVTAG Secretariat: Ruth Parry, Stephen Barnard DHSC Observers (CMO's office): [redacted], Jonathan Van Tam (JVT), [redacted] Invited experts/ presenters: UKHSA: Meera Chand (MCh); University of Edinburgh: Andrew Rambaut (AR); Imperial College, London: Paul Kellam (PK)
Apologies: NA

Contents

Summary of extraordinary meeting

- A short summary of the meeting was signed off by the Chair and sent to CMO's office by 17.00 on 25 November. This is attached at Annex A.

Advice:

Despite substantial current uncertainty about the characteristics of B1.1.529, there are sufficiently worrying signals for the subgroup to advise that:

1. **A large wave of infections that may be sufficient to overwhelm NHS capacity cannot, at this stage, be ruled out.**
2. **Introduction of B.1.1.529 into the UK might have very serious consequences and, therefore, early and aggressive actions to prevent introduction and onward transmission are warranted.**

3. **Actions should be taken to enhance the early detection of B.1.1.529 and, if necessary, to implement containment measures.**

4. **Acceleration of the vaccine boosting campaign should be considered, which might help mitigate some impact of a B.1.1.529 wave, and at a minimum would help control concurrent Delta impact.**

5. **The optimal use of available antiviral products should be reconsidered in light of the new threat posed by B.1.1.529.**

6. **Actions should be taken to enhance the characterisation of B.1.1.529 e.g. computational biology, obtaining live virus samples and constructing pseudoviruses.**

7. **Preparations should be made for the modification of countermeasures i.e. vaccines and monoclonal antibodies.**

Introductions

The Chair welcomed all to the meeting and remind attendees of the confidentiality of the discussion, noting that a brief note would be sent to the CMO that day and the meeting minutes would be prepared and published in due course. It was noted that the aim of the meeting was to provide independent scientific advice so that any policy decisions were made with the full understanding of what is, and is not, known.

The Chair indicated that the meeting had been called to discuss the emergence of the SARS-CoV-2 B.1.1.529 variant, detected in Botswana, South Africa and one case in Hong Kong. Data from South Africa indicated that this was a viable variant and appeared to be spreading.

The Chair applauded the transparency of South Africa in that a number of genomes had been uploaded that day and there had been a Press Conference by the South African Ministry for Health.

1 Data available on the B.1.1.529 variant to date

1.1 MCh noted that the variant was detected on 23 November (uploaded to GISAID). There were numerous mutations in the spike gene, as well as outside of the spike. Initially a small number of genomes from Botswana had been available, with more genomes from South Africa uploaded in the previous two days. There had now been at least one export to Hong Kong.

1.2 The Variant Technical Group (VTG) agreed that the profile of mutations was very concerning, but at the time the likely spread of the variant was not known.

1.3 Data provided in the Press Conference indicated the number of cases as well as the S gene target failure (SGTF) profile that indicated the variant. There had been evidence that there was wider community transmission. As a result of the information provided the VTG had agreed to consider it as a variant under investigation (VUI); this was not, at the time, in the public domain.

1.4 There was not at the time confirmation of phenotypic changes that would indicate that it should be declared a Variant of Concern (VoC). More sequences were being uploaded to GISAID regularly and the VTG would be updating their considerations as needed.

1.5 It was noted that the Delta wave in South Africa was now over, unlike the UK where the number of cases was high, and Delta was the dominant variant. The population in South Africa was likely to be highly immune, in that there was a high level of natural immunity due to recent infection with the Delta variant and there was an ongoing vaccination programme, with high uptake.

1.6 It was noted that infection/outbreaks of B.1.1.529 tended to be amongst younger people, e.g., the cluster in Johannesburg was associated with a university.

1.7 Data from ***WEEKLY TESTING SUMMARY - NICD*** were shared showing the increase in test positivity rates from week 44 (31 October-6 November) through to week 46 (14-20 November), particularly in Gauteng. It was noted that there had been a rapid increase in S gene target failure (SGTF) PCR detections in multiple provinces and that all of the samples collected from Guateng between 12 and 20 November and sequenced, were B.1.1.529.

1.8 WB indicated that the rapid spread was biologically plausible, noting that there were several markers of increased transmissibility. Unlike Delta there were mutations in all four 'Barnes antigenic sites' in the RBD (referring to ***SARS-CoV-2 neutralizing antibody structures inform therapeutic strategies | Nature***), both components of Regeneron would be 'knocked out' as well as the polyclonal response from vaccinees and those who have been infected potentially having reduced neutralising titres

1.9 It was noted that South Africa estimated R to be about 2 (all strains). In South Africa as a whole it was estimated to be 1.4. In Guateng it was estimated to be 1.95. At the same time the reproduction number for Delta was known to be below 1.

1.10 In summary the Chair stated that the group believed it was highly likely that it was a fit virus, probably widespread in South Africa, but had also been picked up in Botswana. It was highly likely to be highly transmissible. With regard to severity, it was noted that most of the detections had been in younger adults, although it was recognised that South Africa is a young population. Hospitalisations were starting to increase, but it was recognised that an increase in cases would lead to an increase in hospitalisations without the infection needing to be any more severe than other strains.

1.11 The Chair indicated that bearing in mind the constellation of mutations, the concern was escape from immunity, however the virus was available, and laboratories were synthesising pseudoviruses. It would be around two weeks before the results of neutralisation assays were available. There were concerns about the possibility of immune escape, but nothing could be said for certain until relevant experiments had been carried out.

2 Discussion of the potential impact of introduction of B1.1.529 into the UK

2.1 JE outlined work that could be done to estimate the size of a potential wave in the UK; it would depend on a combination of actions taken, transmissibility, and immune escape once they were understood. Based on the information available at the time, a large wave in the UK could not be ruled out.

2.2 At this point in time there is a lot of uncertainty about severity and hospitalisation rates.

2.3 It was agreed that introduction of a new variant just before winter and the possibility of co-circulation with influenza could put undue pressure on the NHS and that any action that could be taken prior to a wave of the variant should be considered.

2.4 Measures to enhance the early detection of B.1.1.529 had already been considered by UKHSA and it was noted that a case ascertainment strategy was being developed.

2.5 The acceleration of the vaccine booster programme, using currently available vaccines, by extending to the cohorts that are not already being offered boosters was suggested. This would allow a large proportion of the population to have as a high a level of protection as possible.

2.6 There was discussion of the use of antiviral products. It was noted that there were some antiviral drugs available.

2.7 It was agreed that this was potentially very serious and that all measures should be taken to detect introductions into the UK and slow the spread if possible.

2.8 MCh noted that with regard to awareness-raising there was a briefing with the infectious diseases network that evening.

2.9 MCh noted the forward investigations that could be carried out were limited in the UK in the absence of virus. Pseudovirus work had been triggered and isolates would come in due

course.

3 AOB

3.1 A note will be forwarded for the CMO's meeting at 17.30 today, followed by the full Minutes in due course.

ANNEX A

Brief note of the extraordinary meeting of NERVTAG subgroup on SARS-CoV-2 variant B.1.1.529

Date & Location: 15:00 – 16:00, 25 November 2021 - Via telecon only
In attendance: *NERVTAG Chair:* Peter Horby (PH) *NERVTAG Members:* Julian Hiscox (JHi), John Edmunds (JE), Wendy Barclay (WB), Ravi Gupta (RG) *NERVTAG Secretariat: UKHSA* - Ruth Parry (RP), Stephen Barnard (SB); DHSC - [redacted] *Invited experts/presenters:* UKHSA - Meera Chand (MCh); University of Edinburgh/ COG UK - Andrew Rambaut (AR), Imperial College, London - Paul Kellam (PK) *DHSC Observers:* [redacted], Jonathan Van Tam (JVT)
Apologies: NA

Brief summary of NERVTAG subgroup opinion.

The sub-group considered available information on:

1. The genomic characteristics of B.1.1.529
2. The epidemiology of B.1.1.529 available from genomic surveillance and from the press conference given by the South African Health Authorities this morning.
3. The South African context, with respect to recent prior circulation of SARS-CoV-2 variants and levels of population immunity.

The observations of the NERVTAG sub-committee are as follows:

4. The number of B.1.1.529 cases has rapidly increased in one area of SA (Gauteng). Although B.1.1.529 now represents the dominant genotype in this area, there are likely biases in sampling (over-sampling in areas most affected by B.1.1.529), so the true proportion of cases that are B.1.1.529 in this area is uncertain.
5. The mutations observed in B.1.1.529 include some that are known to be associated with enhanced transmissibility.
6. SA estimates an R-value of 1.9 for B.1.1.529 in Gauteng.

7. B.1.1.529 has a genotype that would lead to failure to detect the S gene target in PCR assays (S gene target failure – SGTF). To the best of the subgroup's knowledge, there are no other prevalent SARS-CoV-2 variants in South Africa (SA) with SGTF.

8. 100% of SGTF samples sequenced in the recent period in SA have been confirmed as B.1.1.529.

9. It is therefore a reasonable assumption, at this stage, that SGTF in SA is currently a reliable marker of the variant B.1.1.529.

10. Samples with SGTF are being detected in multiple provinces of SA.

11. **Conclusion: the subgroup concludes that it is highly likely that B.1.1.529 is a 'fit' virus that is undergoing extensive community transmission in SA, and possibly elsewhere.**

12. The R-value estimate of 1.9 is occurring against a background of high levels of immunity following the recent wave (wave number 3) of Delta variant infections in SA and an active immunisation programme.

13. The multiple mutations observed in the B.1.1.529 spike glycoprotein, the major target for neutralising antibodies (including monoclonal antibodies), are highly likely to result in reduced neutralising ability of antibodies raised to earlier variants and vaccination.

14. Although there is not yet any direct experimental evidence of immune escape, the genotype and the epidemiology in SA are highly suggestive that B.1.1.529 is an antigenically divergent variant that is able to successfully infect previously infected or vaccinated individuals.

15. There are currently insufficient data to make any comments on disease severity associated with B.1.1.529.

16. Whilst we do not know the effect of the B1.1.529 mutations on the vaccine efficacy (VE) against severe disease, it is possible that VE against severe disease could be reduced.

17. **Conclusion: the subgroup concludes that if introduced into the UK, B.1.1.529 would likely be capable of initiating a new wave of infections. We cannot exclude that this wave would be of a magnitude similar, or even larger, than previous waves.**

18. **Conclusion: Although data on disease severity associated with B.1.1.529 are not yet available, a large wave of infections will be accompanied by a wave of severe cases and the subgroup cannot rule out that this may be sufficient to overwhelm NHS capacity**

19. Although computational analyses are ongoing, the multiple mutations observed in the B.1.1.529 spike glycoprotein are likely to render many of the currently available monoclonal antibodies ineffective.

Despite current uncertainty about the characteristics of B1.1.529, there are sufficiently worrying signals for the subgroup to advise that:

20. **Introduction of B.1.1.529 into the UK might have very serious consequences and, therefore, early and robust actions to prevent introduction and onward transmission are warranted.**

21. **Actions should be taken to enhance the early detection of B.1.1.529 in the UK and, if necessary, to implement containment measures.**

22. **Acceleration of the vaccine boosting campaign should be considered, which might provide some residual or significant VE against B1.1.529, and at a minimum would help control concurrent Delta impact.**

23. **The optimal use of available antiviral products should be reconsidered in light of the new threat posed by B.1.1.529.**

24. **Actions should be taken to enhance the characterisation of B.1.1.529 e.g. computational biology, obtaining live virus samples and constructing pseudoviruses.**

25. **Preparations should be made for the modification of countermeasures i.e. vaccines and monoclonal antibodies.**

END

Signed off by Chair, following review by subgroup members. Full Minutes of the meeting will be prepared and published in due course