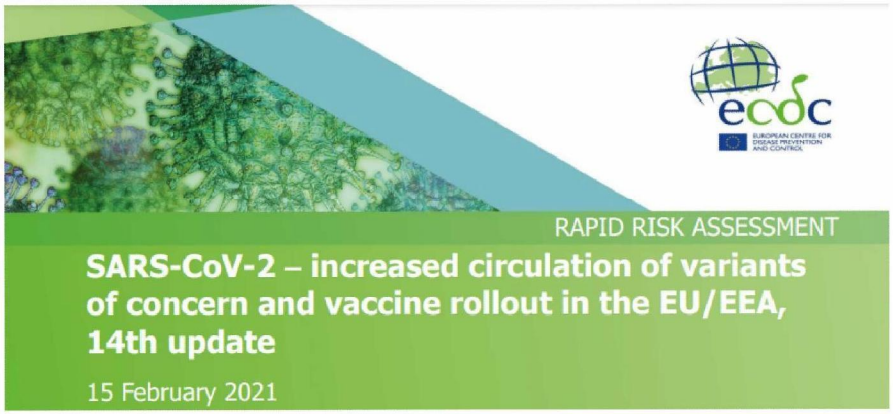
New SARS-CoV-2 variants in the EU/EEA and options for response – rapid risk assessment 15 February

5.1.2e & 5.1.2e, EU/EEA NITAG COLLABORATION MEETING FEBRUARY 18, 2021



RAPID RISK ASSESSMENT

SARS-CoV-2 – increased circulation of variants of concern and vaccine rollout in the EU/EEA, 14th update

15 February 2021

Summary

Several EU/EEA countries have observed a decline in the overall incidence of SARS-CoV-2 in recent weeks, most probably due to the impact of tightened non-pharmaceutical interventions (NPIs). Nonetheless, the epidemiological situation is still of serious concern across the EU/EEA, with the majority of countries still experiencing high or increasing notification rates in older age groups and/or high death rates. Although vaccine rollout has started in all EU/EEA countries, targeting priority groups based on their risk of developing severe disease (the elderly and residents in long-term care facilities) as well as healthcare and other front-line workers, it is still too early to detect an impact on COVID-19 mortality or hospitalisations.

While most countries are currently seeing a decline in overall infections as a response to NPIs, the introduction and increased spread of new SARS-CoV-2 variants first identified in the United Kingdom (B.1.1.7), South Africa (B.1.351) and Brazil (P.1) has raised concerns. As suggested by recent anti-lockdown protests and civil

https://www.ecdc.europa.eu/sites/default/files/documents/RRA-covid-19-14th-update-15-feb-2021.pdf

EUROPEAN
COMMISSION

Brussels, 17.2.2021
COM(2021) 78 final

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE EUROPEAN COUNCIL AND THE COUNCIL

HERA Incubator: Anticipating together the threat of COVID-19 variants

- Rapid detection of variants
- Swift adaptation of vaccines
- Setting up a European Clinical Trials Network
- Fast-tracking regulatory approval of updated vaccines
- Enable upscaling of production of existing, adapted and novel COVID-19 vaccines

Press release | 17 February 2021 | Brussels

Coronavirus: Commission approves second contract with Moderna to ensure up to additional 300 million doses

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Today, the European Commission approved a second contract with the pharmaceutical company Moderna, which provides for an additional purchase of 300 million doses (150 million in 2021 and an option to purchase an additional 150 million in 2022) on behalf of all EU Member States. The new contract also provides for the possibility to donate the vaccine to lower and middle-income countries or to re-direct it to other European countries.

Today's contract with Moderna builds upon the broad portfolio of vaccines to be produced in Europe, including the already signed contracts with BioNTech/Pfizer, AstraZeneca, Sanofi-GSK, Janssen Pharmaceutica NV, Curevac and Moderna. This diversified vaccines portfolio will ensure Europe has access to 2.6 billion doses, once the vaccines have been proven to be safe and effective.

Pfizer and BioNTech to Supply the European Union with 200 Million Additional Doses COMIRNATY®

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February 17, 2021 04:00 ET | **Source:** BioNTech SE

multilang-release

- *New agreement brings total supply to the European Union to 500 million doses, with delivery expected by the end of 2021*
- *European Commission has the option to request an additional 100 million doses*

NEW YORK and MAINZ, GERMANY, February 17, 2021 (GLOBE NEWSWIRE) -- Pfizer Inc. (NYSE: PFE) and BioNTech SE (Nasdaq: BNTX) today announced an agreement with the European Commission (EC) to supply an additional 200 million doses of COMIRNATY®, the companies' COVID-19 vaccine, to the 27 European Union (EU) member states. The EC has the option to request supply of an additional 100 million doses.

This new agreement is in addition to the 300 million doses that have already been committed to the EU through 2021 under the first **supply agreement** signed last year. The additional 200 million doses are expected to be delivered in 2021, with an estimated 75 million to be supplied in the second quarter.

The total number of doses to be delivered to the EU member states by the end of 2021 is now 500 million, with the potential to increase to 600 million based on the option granted in the new agreement.

Assessments of risk due to new VOCs

Due to

- increased transmissibility;
- evidence of increased severity/mortality;
- potential for the existing licensed COVID-19 vaccines to be partially or significantly less effective against some VOCs;
- probability that the proportion of SARS-CoV-2 cases due to B.1.1.7 is high (and possibly also B.1.351 and P.1) will increase

the risk associated with further spread of the SARS-CoV-2 VOCs in the EU/EEA is currently assessed as **high to very high** for the overall population and **very high** for vulnerable individuals.

B.1.1.7 Reinfection and vaccination

- Reinfection rate of 0.7% (95% CI 0.6 – 0.8), no evidence that this was higher than for older strains;
- ~3-fold neutralizing antibody reduction in convalescent sera compared to Victoria-1;
- Almost 10-fold neutralizing antibody reduction in convalescent sera when B.1.1.7 also contained the E484K mutation;
- Despite this reduction, up to 60% of convalescent serum samples are thought to retain functional activity above neutralising threshold. This is also stressed by EMA for some of the vaccines.

B.1.351 Reinfection and vaccination

- Seropositivity to a previously dominant circulating SARS-CoV-2 variant did not confer protection, reinfections occur;
- 10-30-fold neutralizing antibody reduction in convalescent sera compared to previously circulating SARS-CoV-2 variants;
- 10-50% of convalescent serum samples and vaccine sera retaining activity above neutralising threshold, the latter varies by vaccine reported in media or non-peer-reviewed articles

P.1 Reinfection and vaccination

- Very limited data available.
- Reinfections reported in TC/VCs
- Presence of the E484K mutation suggests possible impact on neutralizing antibodies

Vaccine developer	Non-variant and variants of concern			
	Non-variant	B.1.1.7	B.1.351	P.1
BioNTech/-Pfizer				
Efficacy	**95%** (95%CI 90.0 - 97.9) overall efficacy	n.a.	n.a.	n.a
Effectiveness	**94 – 95%** 7 Days after Dose 2 **51.4%** (95%CI -7.2 - 78.0) Day 13-24 after Dose 1	n.a.	n.a.	n.a
Moderna				
Efficacy	**94.1%** (95%CI, 89.3 - 96.8) overall efficacy	n.a.	n.a.	n.a
Effectiveness	n.a	n.a.	n.a.	n.a
Oxford/ AstraZeneca				
Efficacy	**59.5%** (95%-CI 45.8 - 60.7) overall efficacy	**74.6%** (95%CI 41.6 - 88.9) (compared to non-B.1.1.7 lineages: 84% (95%CI 70.7 - 97.4)	**21.9%** (95%CI -49.9 – 59.8)	n.a
Effectiveness	n.a	n.a.	n.a.	n.a
Johnson & Johnson (1-dose)**				
Efficacy	**66% (Press release)** overall efficacy	n.a.	**57% (Press release)** overall efficacy	n.a
Effectiveness	n.a.	n.a.	n.a.	n.a
Novavax**				
Efficacy	**95.6% (Press release)** overall efficacy	**89.3% (Press release)** (95%CI 75.2 - 95.4)	**49.4% (Press release)** (95%CI 6.1-72.8)	n.a
Effectiveness	n.a.	n.a.	n.a.	n.a

Options for response

Based on the current epidemiological situation in the EU/EEA with the increased circulation of more transmissible variants:

- immediate, strong and decisive public health interventions are essential to control transmission and safeguard healthcare capacity;
- layered NPIs to be strengthened and maintained in the coming months in order to reduce SARS-CoV-2 incidence to the lowest levels possible, thereby also minimising the opportunities for new variants to emerge.

Options for response cont

- Optimising the implementation of NPIs, including community use of facemasks and school settings, is essential;
- Test and trace approaches, including strong surveillance and sequencing, remain the cornerstones of the response;
- Travel should not be undertaken by people who are ill or who have had recent contact with COVID-19 cases;
- Furthermore, ECDC recommends that non-essential travel should be avoided as part of general physical distancing measures in the community;
- In time, targeted and robust vaccination programmes will enable the easing of NPIs.

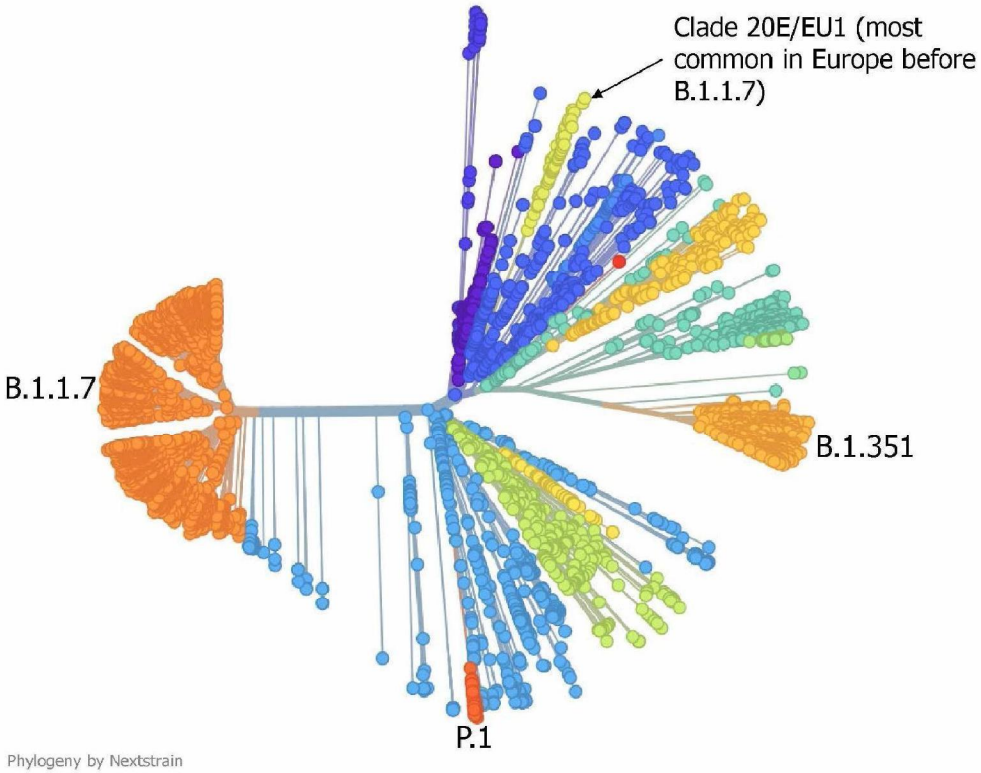
Options for response cont

- Variants against which current licensed vaccines might have a reduced efficacy, as observed for some vaccines with the B.1.351 variant first identified in South Africa, will probably continue to emerge in the future;
- This should be mitigated by designing next-generation vaccines with mutated spike sequences and using alternative viral antigens;
- Consideration should also be given to their use either as booster doses for those vaccines which have already been developed and are being administered, or, if needed, for the primary series.

Options for response cont

- Increasing levels of pandemic fatigue need to be properly addressed as a matter of urgency if further waves of infection are to be avoided and population compliance is to be maintained;
- Public expectations about the likelihood of easing restrictions need to be carefully managed;
- To facilitate this, authorities should make systematic efforts to ensure that they have a good understanding of community perceptions of the pandemic, the NPIs in place and COVID-19 vaccine acceptance through ongoing behavioural research.

Variants of concern, phylogeny with genetic background



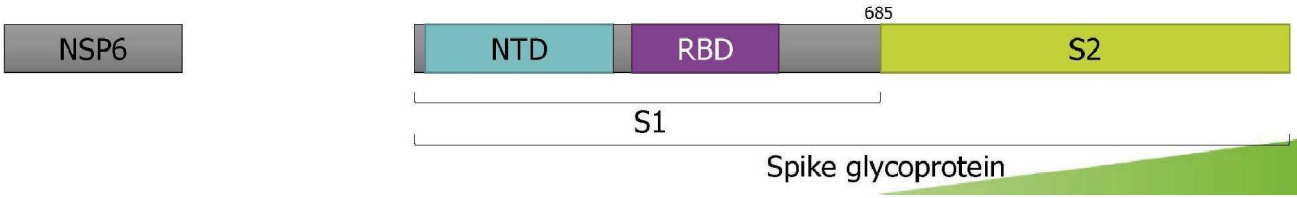
Phylogeny by Nextstrain

- The variants of concern detected so far are not closely related and have evolved independently
- Through convergent evolution they have acquired some common mutations that seem to be functionally relevant

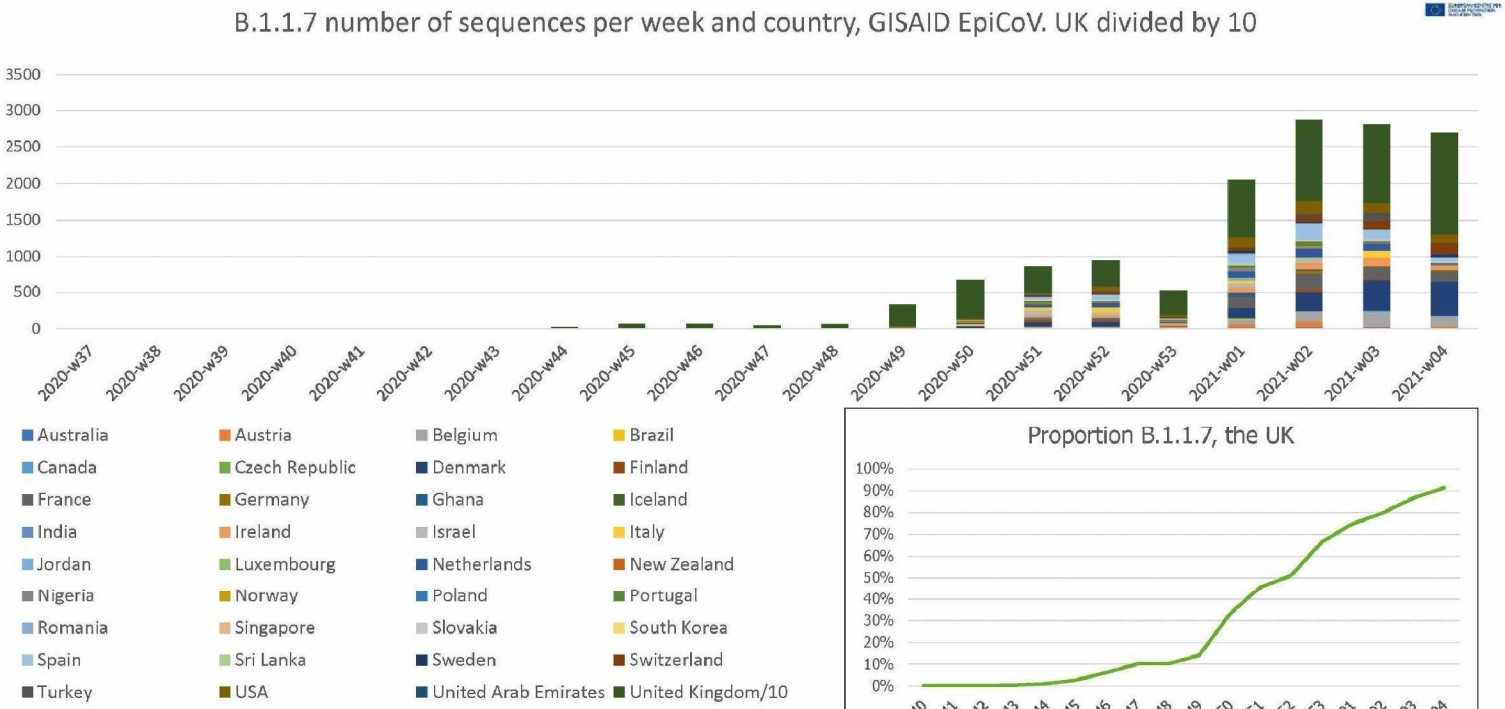
Mutations of interest

- The variants of concern all have a high number of spike protein changes
- The most important epitopes for nAbs seem to be located in the spike NTD and RBD
- Changes at sites that are common between VOCs are highlighted in bold below
- The NSP6 deletion is intriguing, but the functional effect of this deletion is unknown

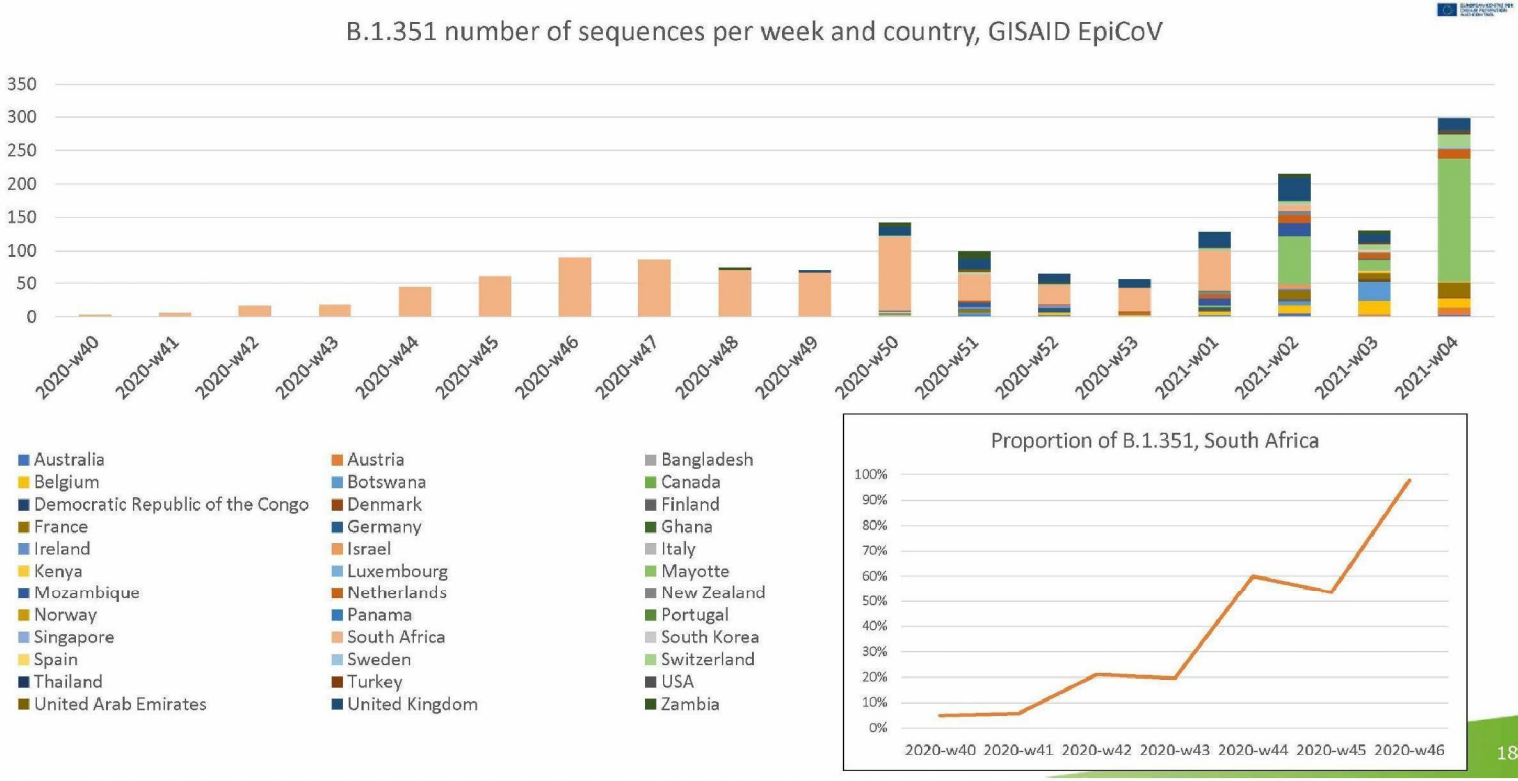
Variant	NSP6	S1: NTD	S1:RBD	S1/S2	S2
B.1.1.7 (+E484K)	**Δ106-108**	Δ69-70 Δ144	**N501Y, (E484K)**	A570D, **D614G**, P681H	T716I, S982A, D1118H
B.1.351	**Δ106-108**	L18F, D80A, D215G, Δ242-244, R246I	**K417N, E484K, N501Y**	**D614G**	A701V
P.1	**Δ106-108**	L18F, T20N, P26S, D138Y, R190S	**K417T, E484K, N501Y**	**D614G**, H655Y	T1027I, V1176F



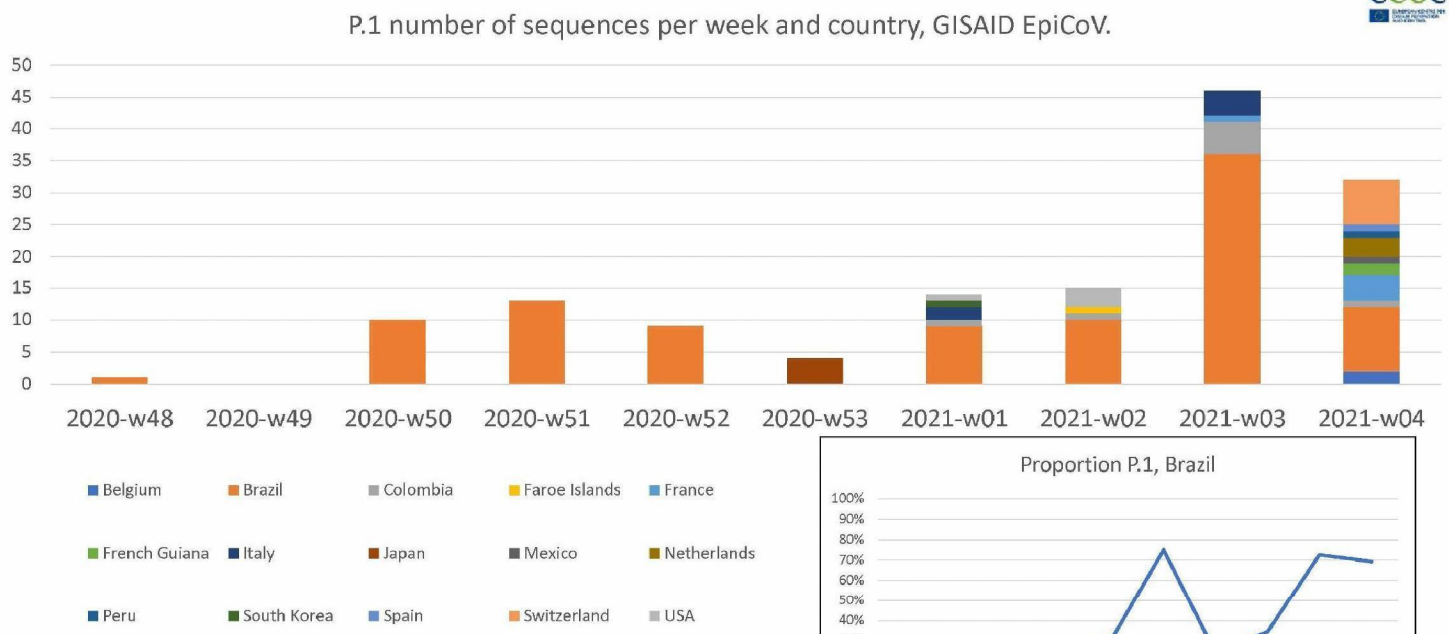
B.1.1.7 (and B.1.1.7+E484K), first detected in the UK, sequences over time



B.1.351, first detected in South Africa, sequences over time

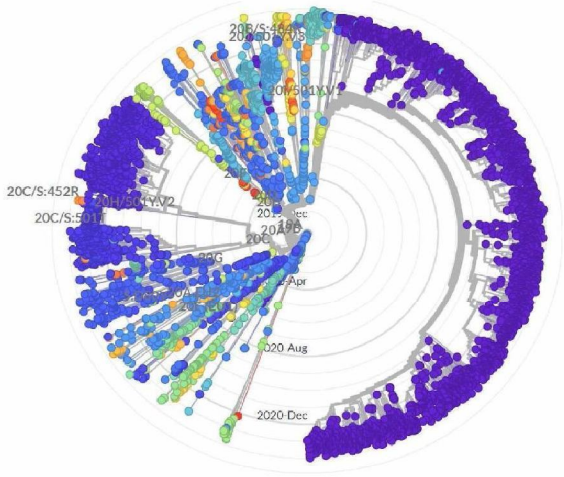


P.1, first detected in Brazil, sequences over time



Variants of interest

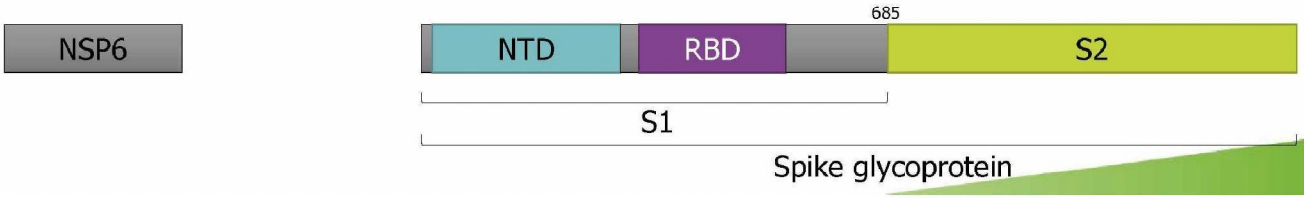
- In addition to the current variants of concern, many other variants are circulating
- Monitoring of variants with potential to be of concern is important



WGS is used to identify variants of interest

- WGS is used to put a label on variants so that we can assess if they are associated with changes in virological and epidemiological properties
- WGS is used to assess whether there are genetic similarities between variants, that could imply similar properties
- WGS is used to find unexpected mutations or combinations of mutations that could warrant further investigations
- More knowledge about genotype to phenotype associations increases the power of WGS

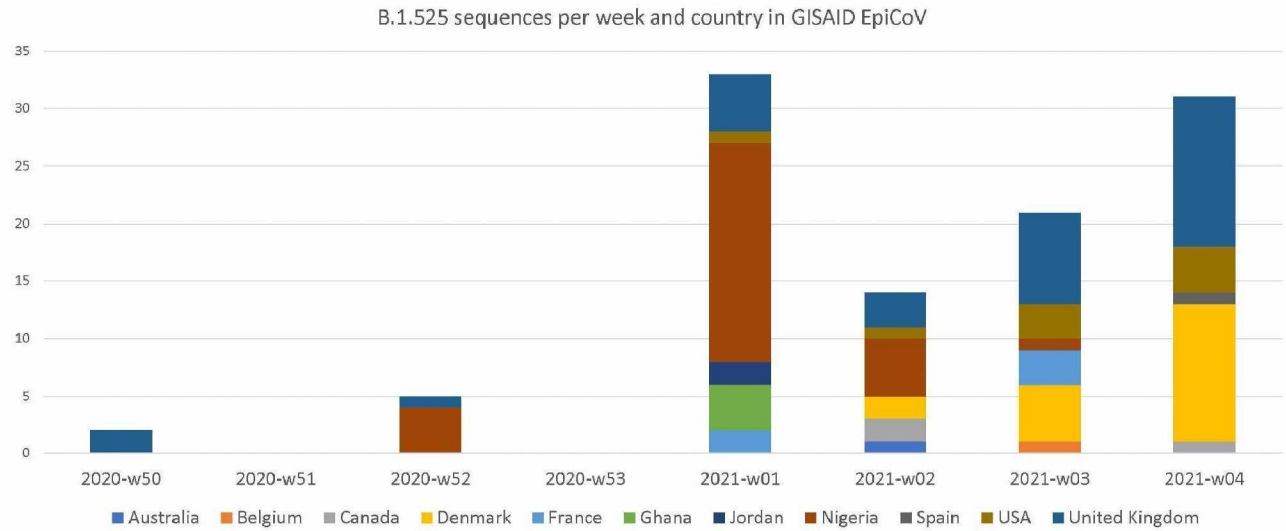
Variant	NSP6	S1: NTD	S1:RBD	S1/S2	S2
B.1.1.7 (+E484K)	**Δ106-108**	Δ69-70 Δ144	**N501Y, (E484K)**	A570D, **D614G**, P681H	T716I, S982A, D1118H
B.1.351	**Δ106-108**	L18F, D80A, D215G, Δ242-244, R246I	**K417N, E484K, N501Y**	**D614G**	A701V
P.1	**Δ106-108**	L18F, T20N, P26S, D138Y, R190S	**K417T, E484K, N501Y**	**D614G**, H655Y	T1027I, V1176F
B.1.525	**Δ106-108**	Q52R, A67V, **Δ69-70 Δ144**	**E484K**	**D614G,** Q677H	F888L
A.23.1		R102I, F157L	V367F, **E484K**	Q613H, **P681R**	
Novel (A+N501Y)		**L18F**	L452R, **N501Y**	A653V, **H655Y**	D796Y, G1219V,
Novel (A+N501T)		**Δ69-70**	**N501T**	**H655Y**	



Variant B.1.525

- Spike Q52R, A67V, **69-70del**, **144del**, **E484K**, D614G, Q677H, F888L
- Reported by Denmark in EWRS (they have observed an increase in the last few weeks)
- First detected by the UK, 15 December 2020
- Several mutations found in other VOCs, but lacking N501Y
- E484K is likely to be associated with reduction in neutralisation by antibodies

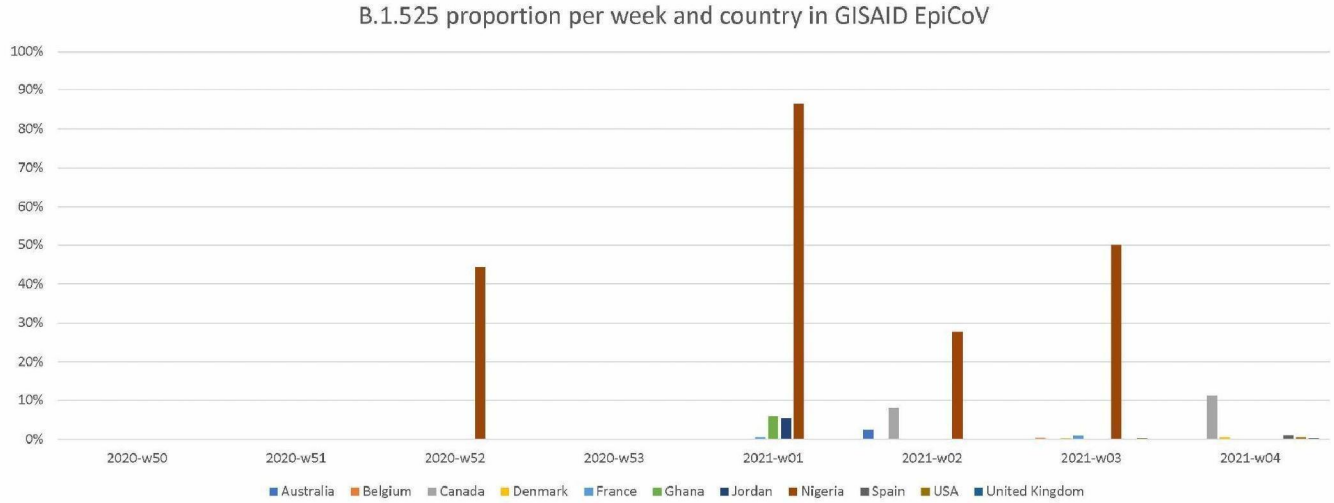
Variant B.1.525, cases over time



Denmark is the only country where a clear increasing trend can be observed (but there may be a lack of timely data from other countries)

Wide geographic distribution, most sequences from Nigeria, the UK and Denmark

Variant B.1.525 as proportion of all sequences

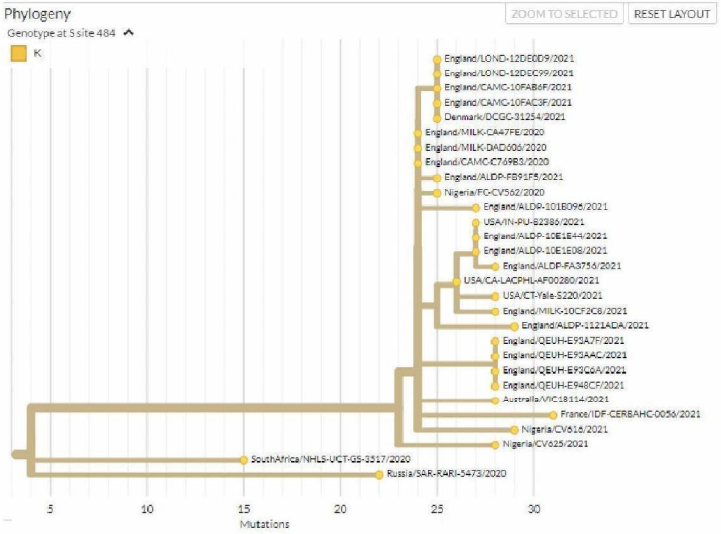


Indication that this variant is already common in Nigeria

Travel can then explain the wide geographic distribution

Limitation: Unknown sampling frame and low number of samples in Nigeria (N=147 since December 15)

Variant B.1.525 phylogeography



Some indication from the phylogeny that the origin might be Nigeria

Recent common ancestor, estimated to 29 October by Nextstrain

Long branch (17 substitutions, 3 deletions) separating it from previous variants

Carries the same 3 amino acid deletion in NSP6 (ORF1a Δ3675-3677, NSP6 Δ106-108) as all VOCs reported so far

Summary

Variants of SARS-CoV-2 are already having a significant impact on the pandemic

- Increased transmissibility
- Changes in infection severity
- Reduction in neutralisation by antibodies

Monitoring of these variants is and will continue to be important to stay proactive when new variants of concern emerge