Genomic surveillance of SARS-CoV-2 in Belgium

Report of the National Reference Laboratory (UZ Leuven & KU Leuven)

Situation update – 16th of March 2021
(report 2021_18)

Executive summary

8.743 Belgian sequences of SARS-CoV-2 are currently available in open access on GISAID, among which 4.545 are unbiased samples collected after the 1st of January 2021 in the context of baseline surveillance.

For baseline surveillance samples collected during the weeks of 1st and 8 of March 2021, 20I/501Y.V1 represented 69,1%, 20H/501Y.V2 represented 5,5% and 20J/501Y.V3 represented 2,6% of all samples analysed.

Previous reports can be downloaded using the following link:
https://www.uzleuven.be/nl/laboratoriumgeneeskunde/genomic-surveillance-sars-cov-2-belgium

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1. International context

Since the end of 2020, 3 variants of concern (VOCs) have arisen independently of one another in the United Kingdom (20I/501Y.V1), South Africa (20H/501Y.V2) and Brazil (20J/501Y.V3). These variants harbour several mutations and deletions associated with (or investigated for) higher infectiousness and immune escape. All variants are spreading internationally and have been detected in Belgium. Another variant of interest (VOI) named B.1.525 shows a high number of mutations in the S1 region of the Spike protein. It has initially been described in Nigeria, but has since then been described in a least four continents.

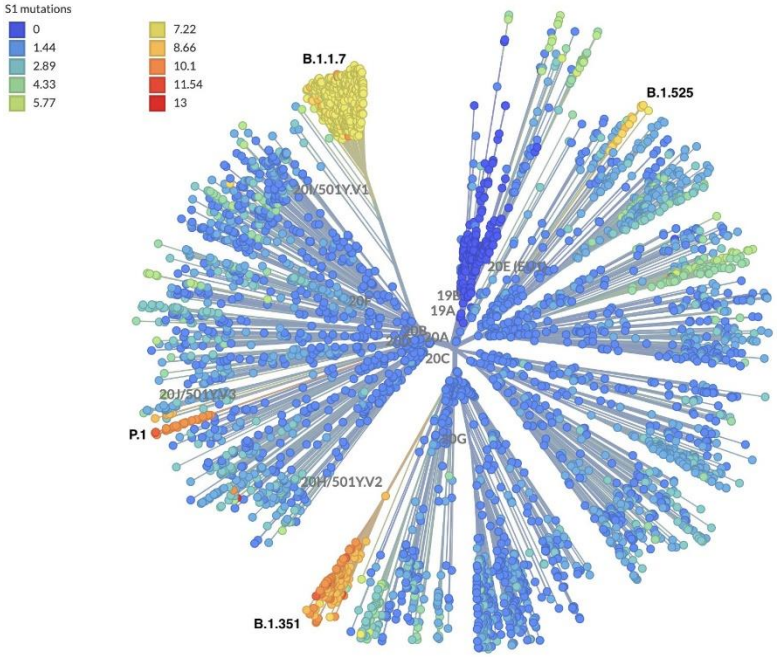

Figure 1: Mutation in the S1 region of the Spike protein may modify receptor binding and may contribute to antigenic drift. Variants of concern (VOCs) have shown excess S1 mutations as illustrated by the colour code.

SARS-CoV-2 lineage B.1.1.7 (501Y.V1) was first detected in the UK in September 2020 and has subsequently spread to many countries around the world. Several studies have established that this VOC is more transmissible than pre-existing variants but had not until recently identified whether it leads to any change in disease severity.

A study performed in the United Kingdom and published on 15/03/2021 reported that the hazard of death associated with this variant is 55% (95% CI 39–72%) higher compared to non-VOC strains. This corresponds to the absolute risk of death for a 55–69-year-old male increasing from 0.6% to 0.9% (95% CI 0.8–1.0%) within 28 days after a positive test in the community. This study concludes that this VOC is not only more transmissible than pre-existing SARS-CoV-2 variants but may also cause more severe illness.

(https://www.nature.com/articles/s41586-021-03426-1)

The situation in Brazil, where 501Y.V3 is widely spreading, is currently very serious (increase of cases, saturation of hospitals). The situation in South-Africa, where 501Y.V2 has emerged, is currently stable after a strong decline since the start of the year.

This week, a number of related clusters of infections caused by a variant of interest (VOI) belonging to the clade 20C has been reported from Lannion (Brittany, France). This variant harbours a number of mutations in the spike protein (S:H66D, S:G142V, S:D215G, S:V483A, S:D614G, S:H655Y, S:G669S, S:Q949R, S:N1187D) and deletions (ORF6 gene (AA position 23 to 31) and S gene (Y144-)). Some reports suggest that some PCR kits targeting the S gene seem to miss the detection of this VOI, possibly due to the modification of the genetic targets. This issue will be further documented, and additional information will be sent to clinical laboratories if the performance of certain diagnostic assays is confirmed to be impacted. Based on the current information available, we do not anticipate a decrease in performance of most multiplex assays used in Belgium.

2. Baseline surveillance

Since support was offered by the federal government at the end of December 2020, both the temporal coverage (number of sequencing analyses performed per week) and geographical coverage (residence of the patients sampled) have improved significantly. Currently, 8.743 Belgian sequences are available on GISAID.

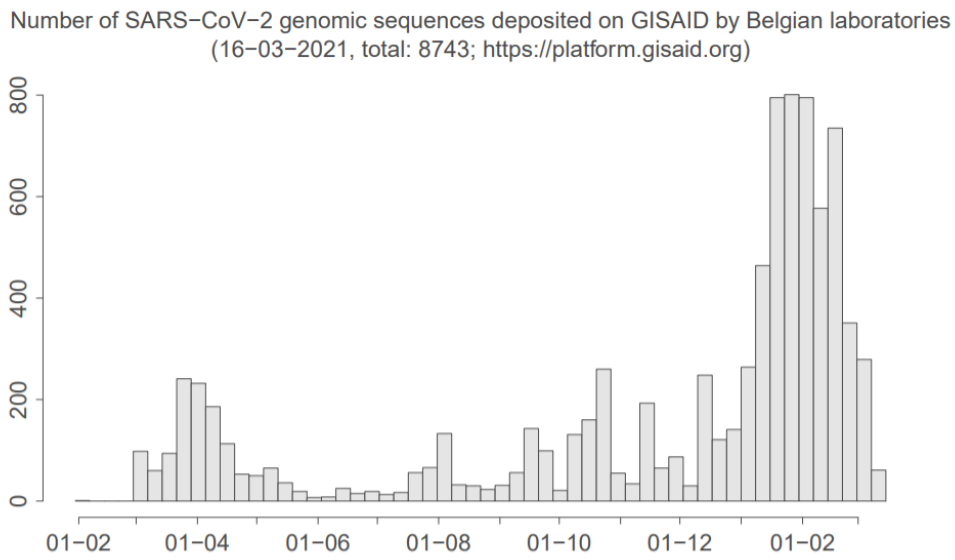

Figure 2: *Number of sequences of SARS-CoV-2 deposited on GISAID per sampling date (baseline surveillance and active surveillance)*

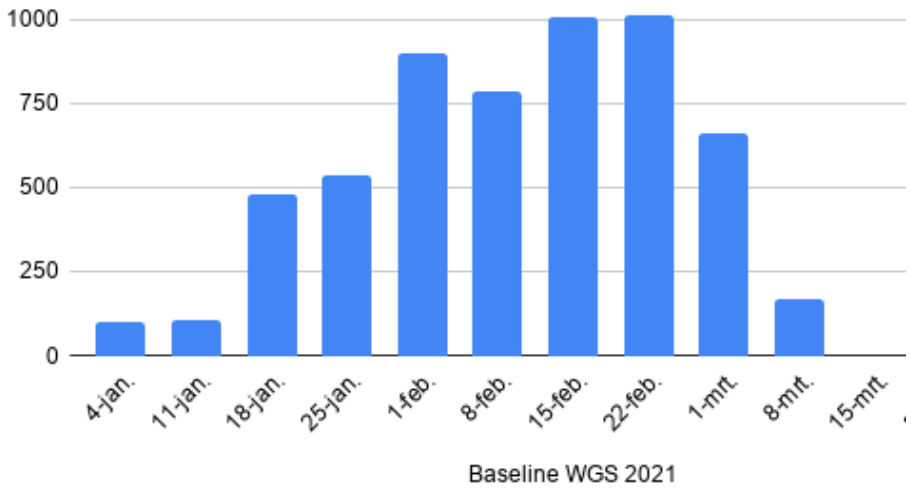

Figure 3: Number of baseline WGS tests performed per sampling date since week 1 of 2021

During the last 74 days (starting on the first of January 2021), we could follow at the level of the federal platform the evolution of the share SGTF (S gene target failure) samples.
The different regions of the country followed a similar evolution despite slight differences observed.

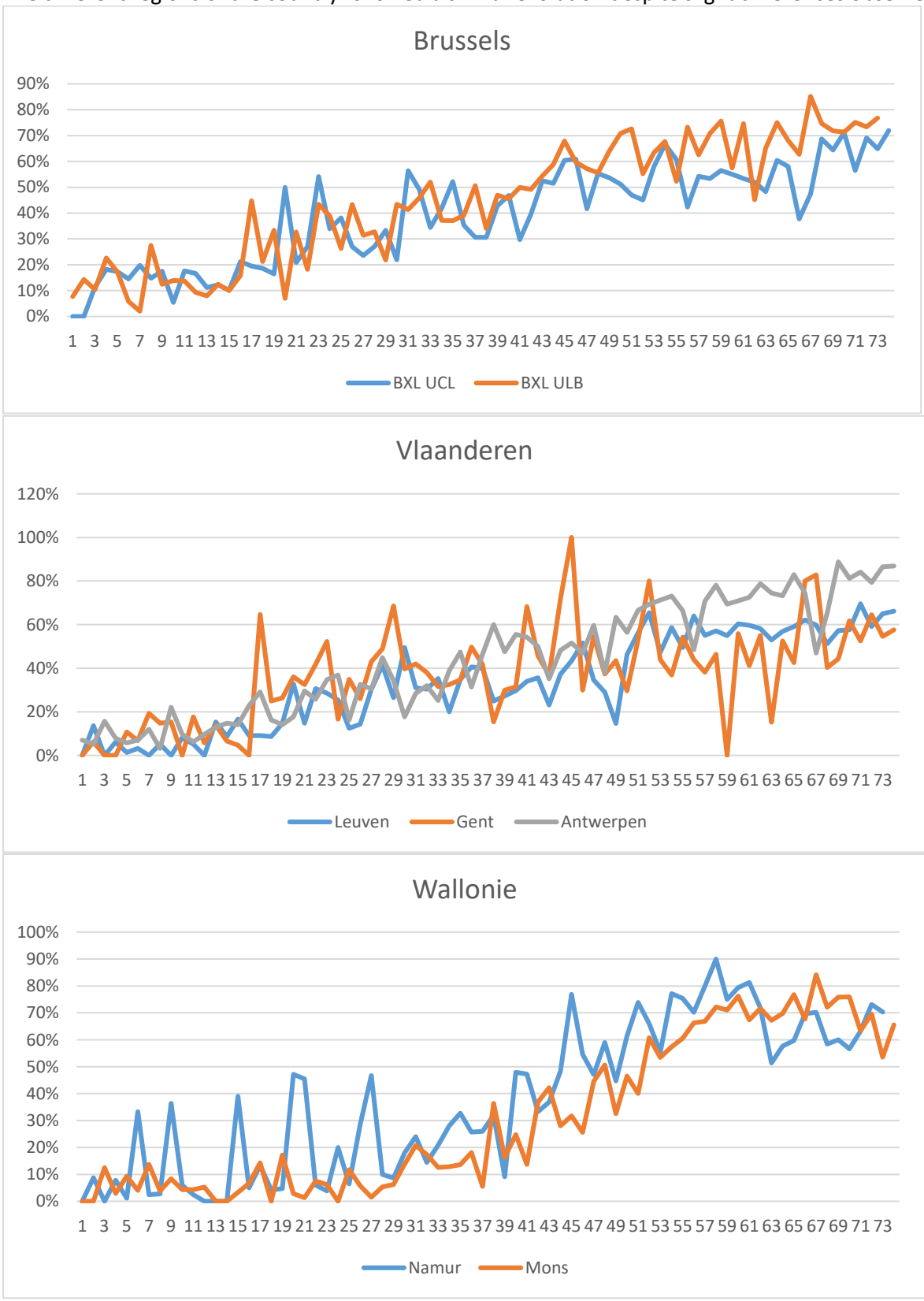

Figure 4: Evolution of SGTF in the different regions of the country since 1st of January 2021 (74 days)

In the results reported by 7/8 federal platforms, both the share and the total amount of 501Y.V1 continue to increase. The increase of 501Y.V1 is sharper than the general increase (total number of cases diagnosed among federal platform laboratories). We cannot at this stage exclude an evolution towards an exponential phase in the coming days and weeks, but it seems clear that the future epidemiological evolution in our country will be "pushed" by the underlying increase of 501Y.V1. This uncertain future evolution should be seen as a window of opportunity to strengthen further the disease control strategies in place (extended testing criteria, testing of low-risk contacts, limitation of large or sustained transmission events), to eventually prevent a phenomenon which is now happening in other European countries.

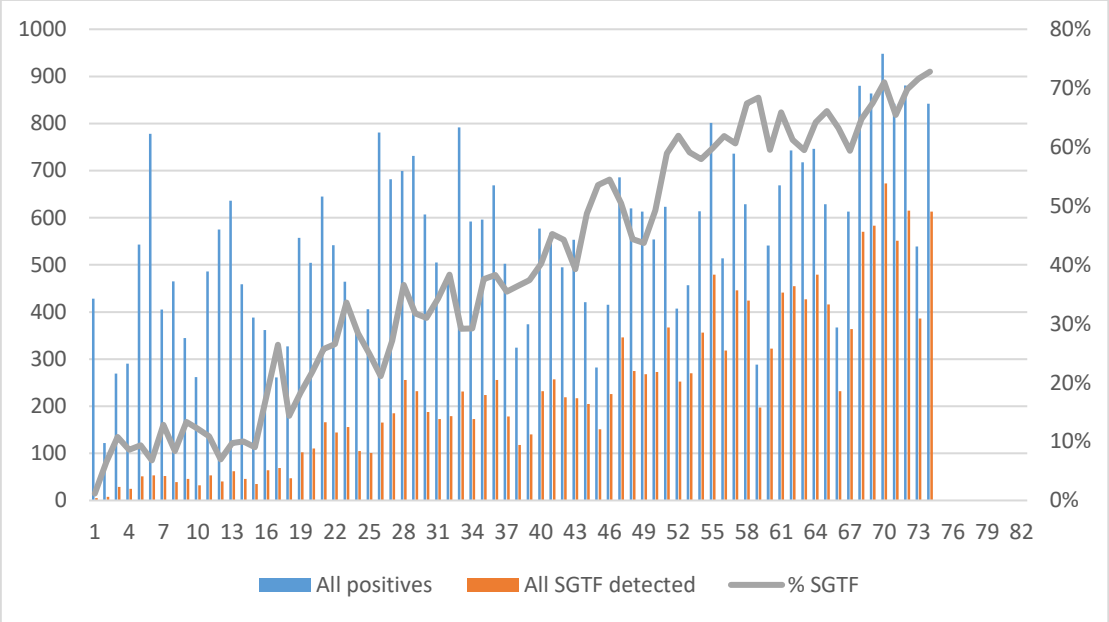

Figure 5: Evolution of the number of positive samples detected (blue, increasing), the number of SGTF samples detected (orange, increasing faster) and the proportion of SGTF among all samples detected (increasing).

3. Monitoring of VOCs in Belgium

After a constant rise in proportion starting from January 2021, the majority of new SARS-CoV-2 infections in Belgium are currently associated with a VOC, principally 501Y.V1. This phenomenon had not translated until recently into a significant rise of cases. We may be currently observing a disruption in this equilibrium since a few days, as Sciensano reported an increase of +21% between the week starting 27/2/2021 and the week starting 27/3/2021.

For samples collected during the weeks of 1st and 8 of March 2021, 20I/501Y.V1 represented 69,1%, 20H/501Y.V2 represented 5,5% and 20J/501Y.V3 represented 2,6% of all samples analysed.

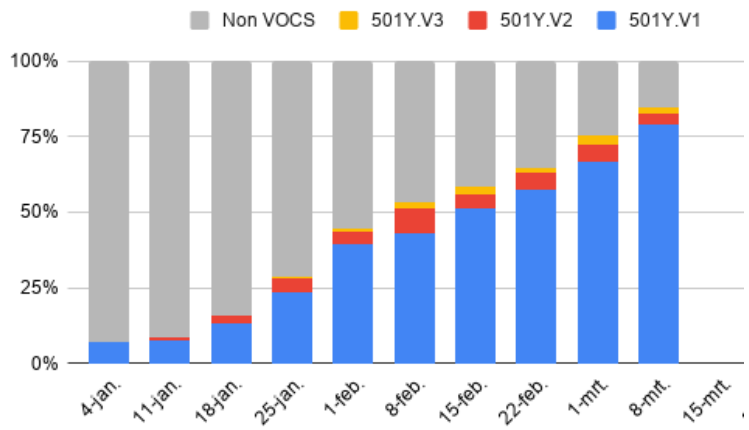

Figure 6: Share of VOCs circulating in Belgium as measured through baseline WGS tests performed per sampling date since week 1 of 2021. Colour code: Non-VOCs (grey), 501Y.V1 (blue), 501Y.V2 (red) and 501Y.V3 (yellow).

4. Co-circulation of VOCs in Belgium

Since the 1st of January 2021, we observe in all provinces of the country a certain level of co-circulation of the different VOCs, although local differences are observed. This period represents a situation with limited competition between the different VOCs, so we cannot yet state on definitive competitive advantage between VOCs. Now that VOCs represent >75% of circulating strains, it will be important to follow how these variants co-evolve the under current selective pressure (contact restrictions, partial herd immunity and stepwise rollout of different vaccines).

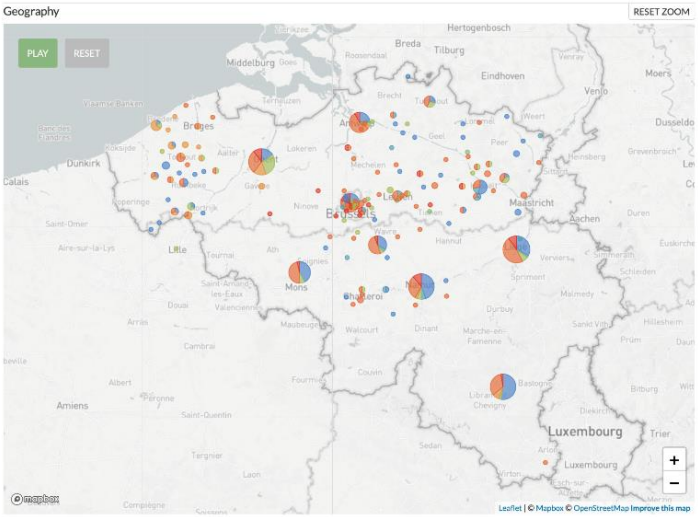

Figure 7: WGS coverage per province since for the period 01/01/2021-15/3/2021 based on sequences available on GISAID. 501Y.V1 (dark orange), 501Y.V2 (light orange) and 501Y.V3 (red) co-circulate at different levels in many areas of Belgium.

In complement to the WGS-sequencing based surveillance performed on approximately 5%-10% of the strains collected in a large network of sentinel laboratories, we started implementing reflex VOC PCRs in the federal platform laboratories. We designed this PCR to target genetic markers of convergent evolution (S:N501Y, S:E484K, S:K417N/T) which allows to reliably detect and characterize the VOCs currently circulating in the country, and to potentially capture further emerging VOCs as they will probably harbour one or several of these genetic markers. The results of our technical validation have been presented to all clinical laboratories of the country. Communications at the European level (ECDC) and global level (Genomeweb) are also programmed. We have suggested to the other federal platform laboratories to introduce this assay. Because these tests can be performed daily and at a relatively low cost in highly automated laboratories, we consider that this new instrument will be a key instrument to better understand the determinants of competition between the different VOCs during the scale-up of the vaccination campaign.

Sample date	4 to 14 March 2021	
Federal platform Lab	UZ Leuven/KU Leuven	
Number of tests performed	486	
501Y.V1	363	74,7%
501Y.V2	6	1,2%
501Y.V3	19	3,9%
Non Voc	82	16,9%
WGS confirmation needed	16	3,3%

5. 501Y.V1 (B.1.1.7)

The 501Y.V1 epidemic in Belgium is characterized by multiple parallel introduction events in a short period of time (end 2020 – start 2021). Despite wide testing of returning travellers from UK and other countries, this situation led to multiple local clusters and a rapid shift with regard to circulating viral populations. This variant represented 70% of infections diagnosed during the first 15 days of March 2021 and represents 75-80% of new infections occurring today.

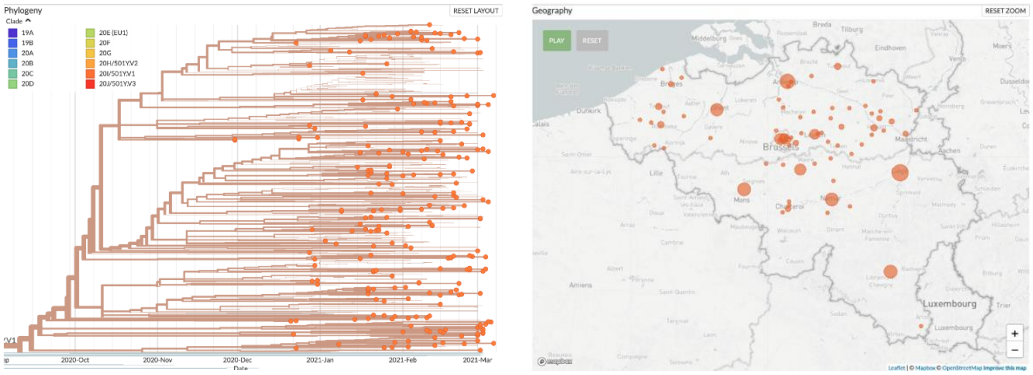

Figure 8: Multiple parallel introductions of 501Y.V1 leading to numerous secondary clusters and a rapid replacement (>75%) of circulating viral strains after 3,5 months.

6. 501Y.V2 (B.1.351)

The 501Y.V2 epidemic in Belgium is characterized by a limited number of parallel introductions among which three have led to secondary clusters, still localized in the provinces of West Flanders and Luxembourg. The NRC has been informed to date of two post-vaccination outbreaks related to 501Y.V2, a phenomenon that will need to be further documented and monitored considering that this VOC is associated with a decrease of vaccine efficacy.

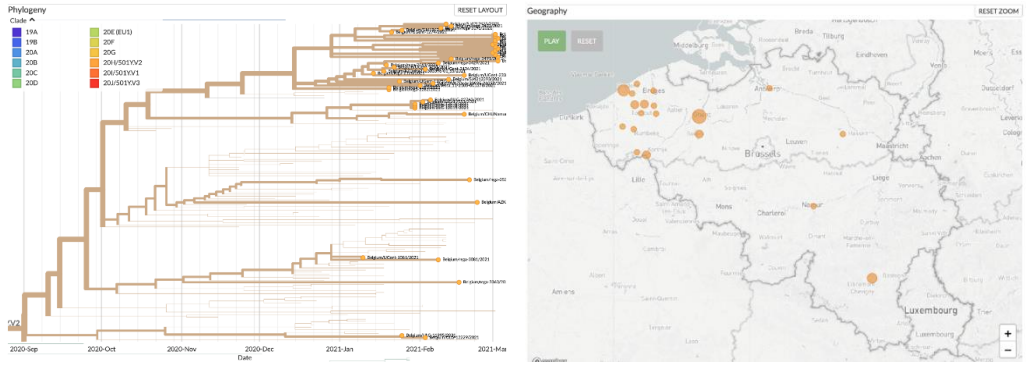

Figure 9: Limited number of parallel introductions of 501Y.V2 leading to three secondary clusters. This VOC represented 5,5 % of infections diagnosed during the 15 first days of March 2021.

7. 501Y.V3 (P1)

The 501Y.V3 epidemic in Belgium is characterized by two parallel introductions and led to one large secondary cluster with two subgroups of strains (it is not yet clear is the common ancestor between these two groups resulted from a transmission in Belgium), dispersed among several provinces of the country. The rapid spread in different provinces of this variant suggests ongoing community transmission, which should be considered as alarming considering the potential immunological and epidemiological consequences if this variant had to become dominant in the coming months without a large vaccination coverage to mitigate its effects.

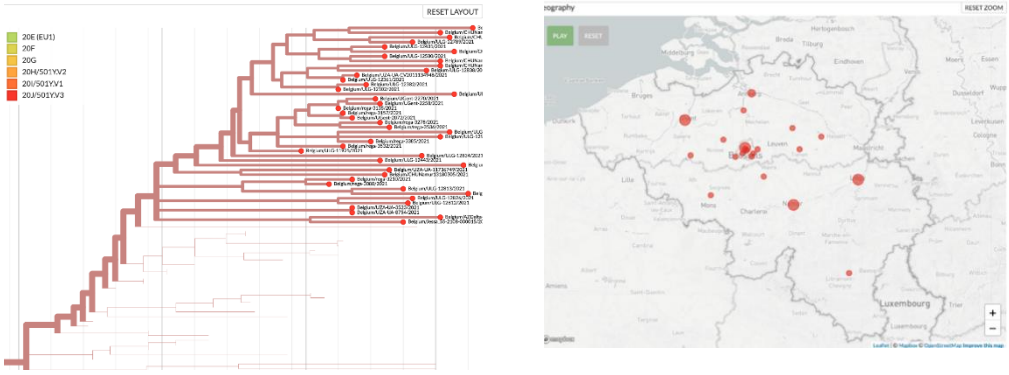

Figure 10: One (possibly two) parallel introduction(s) of 501Y.V3 leading to a diffuse community transmission across different provinces. This VOC represented 2,6% of infections diagnosed during the 15 first days of March 2021.