Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update – 16th of February 2021
(report 2021_11)

Executive summary

Genomic surveillance in Belgium is organised around 3 different arms aiming to monitor the emergence and the further spread of specific viral populations (variants of concern, VOCs) which may impact disease control and/or vaccination strategies.

Through "baseline surveillance", an unbiased selection of positive samples from 24 sentinel labs (selected based on geographical dispersion and diversity of clinical patterns) are analysed in designated sequencing platforms. Currently, 5.476 Belgian sequences are available on GISAID, among which 746 were uploaded during the last week. During week 5 and week 6, 552 samples have been sequenced as part of the baseline surveillance, among which 214 were 20I/501Y.V1 (39%), 27 were 20H/501Y.V2 (5%) and 2 (total of 4 sequences overall) were 20J/501Y.V3 (0,4%).

Active surveillance initiatives aim to detect and characterize (emerging) VOCs in particular situations such as returning travellers (detection of VOCs), local outbreaks (genotyping of a proportion of positive samples), re-infections and post-vaccination infection (full characterization of the genome and study of potential immune escape mechanisms). All clinical laboratories in the country are involved in this network, at least in the identification and referral of the above samples.

The progressive replacement of non-VOC viral strains by more transmissible strains did not result to date in a disruption of the epidemic plateau observed in Belgium since several weeks. This is probably due to a combination of active public health response and limited number of social interactions in the population.
VOCs harbouring the S:E484K mutation (impacting the efficacy of some vaccines) are expected to become more prevalent in the coming months due to the selection pressure consequent to partial herd immunity and stepwise vaccination rollout.

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Table of content

1. International context

Since the end of the year, 4 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 and P.2). These variants harbour several mutations and deletions associated with higher infectiousness and immune escape. All variants are spreading internationally, with 3 VOCs having been detected to date in Belgium (20I/501Y.V1, 20H/501Y.V2 and 20J/501Y.V3).
Together with other mutations of concern, the E484K mutation in the S gene is associated with immune escape mechanisms and causes a possible decrease of efficacy of some vaccines. This mutation is always present in 20H/501Y.V2 and 20J/501Y.V3. It was initially not described in 20I/501Y.V1, but recent reports from the UK highlight independent events of acquisition of this mutation.

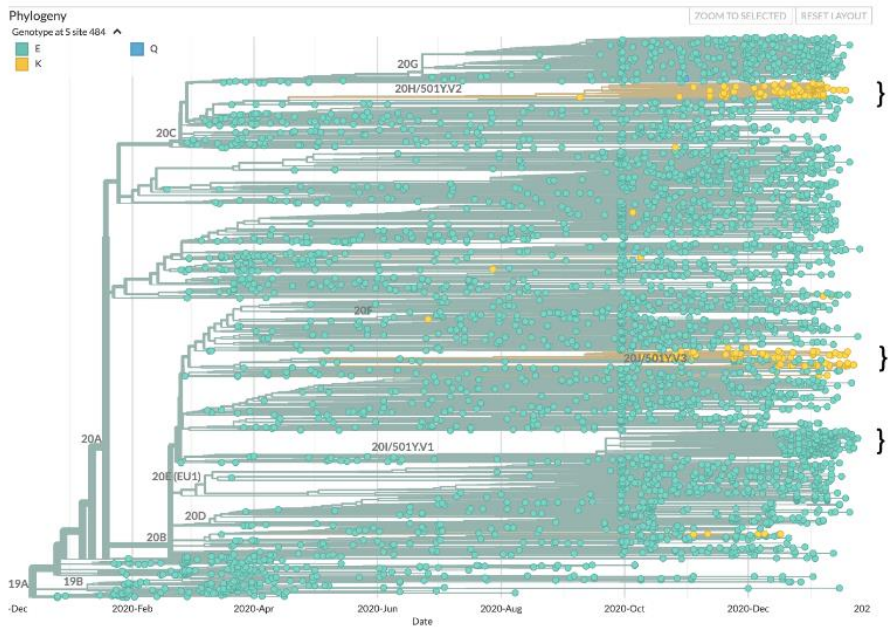

Figure 1: Global view of the S:E484K mutation responsible for partial immune escape, including diminished activity of some vaccines. This mutation is systematically present in variant 20H/501Y.V2 (yellow cluster on the top) and the 20J/501Y.V3 and P.2 VOCs which have emerged in Brazil (yellow cluster in the middle) and has recently emerged among a limited number of 20I/501Y.V1 (third cluster) variants circulating in the UK.

The S:K417N and S:K417T mutations located in the receptor binding domain (RBD) of the S gene are associated with respectively the 20H/501Y.V2 and the 20J/501Y.V3 VOCs. There is no mutation observed in this position for the 20I/501Y.V1 and the P.2 VOCs.

Based on the association of a limited number of genetic markers, it is therefore possible to provide two types of information:

- A combination of tests that can highlight the presence of a VOC and would be able to distinguish 501Y.V1 (more transmissible) from the other VOCs (more transmissible and associated with immune escape mechanism). Such test would incorporate the E484K mutation in association with N501Y mutation (or del69) and would be sufficient to rapidly screen high risk populations such as returning travellers. Such test would need to be followed by sequencing if only one of the two markers would be positive.

- A combination of tests that would allow to perform a presumptive genotype based on a number of mutations listed in the table below, and that would therefore be considered as a reliable and cost-effective alternative to further increase of WGS coverage for precisely monitoring the epidemiological evolution of each VOC during the vaccination roll-out.

	B.1.1.7	**B.1.351**	**B.1.1.28.1 P.1**	**B.1.1.28.2 P.2**
Alternate name	20I/501Y.V1	20H/501Y.V2	20J/501Y.V3	
Mutations	23	21	17	17
Spike mutations	8	9	10	10
Key mutations	E69/70 deletion, N501Y, P681H, 144Y deletion, A570D	E484K, K417N, N501Y, orf1b deletion	E484K, K417T, N501Y, orf1b deletion	E484K, N501Y, orf1b deletion
Other mutations	T716I, S982A, D1118H	D80A, D215G, A701V	L18F, T20N, P26S, D138Y, R190S, H655Y, T1027I	?
Transmissibility	>45% increased	Not established	Not established	Not established
Lethality	Not resolved	?	?	?
Vaccine efficacy reduction	Partial	Yes, reduced in 3 vaccine trials Limited efficacy with Astra Zeneca	Likely Not established	Likely Not established

2. Baseline surveillance

Since support was offered by the federal government end of December 2020, both the temporal coverage (number of sequences performed per week) and geographical coverage (number of collection sites) have improved. Currently, 5.476 Belgian sequences are available on GISAID, among which 746 were uploaded during the last week.

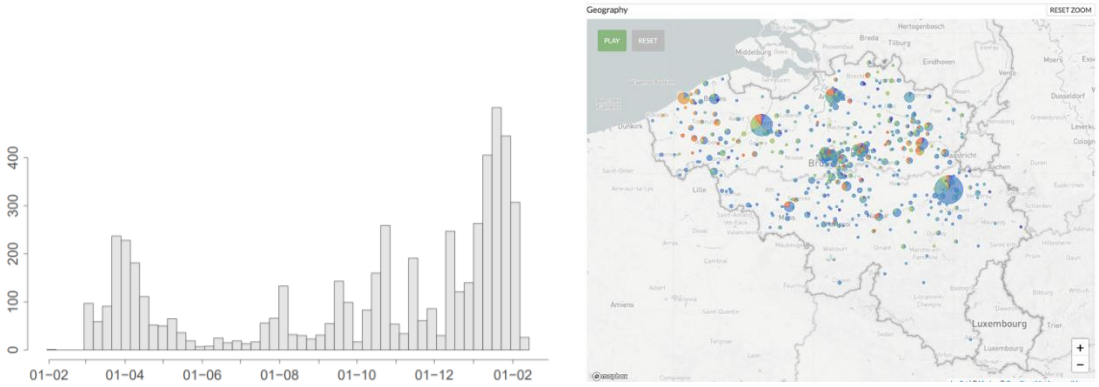

Figure 2: Temporal coverage since the first case was diagnosed in the country and origin of recent Belgian sequences deposited on GISAID.

For baseline surveillance samples collected during week 5 and week 6, a total of 552 sequences are available, among which 214 (39%) were 501Y.V1, 27 (5%) were 501Y.V2. and 2 were 501Y.V3 (0,4%).

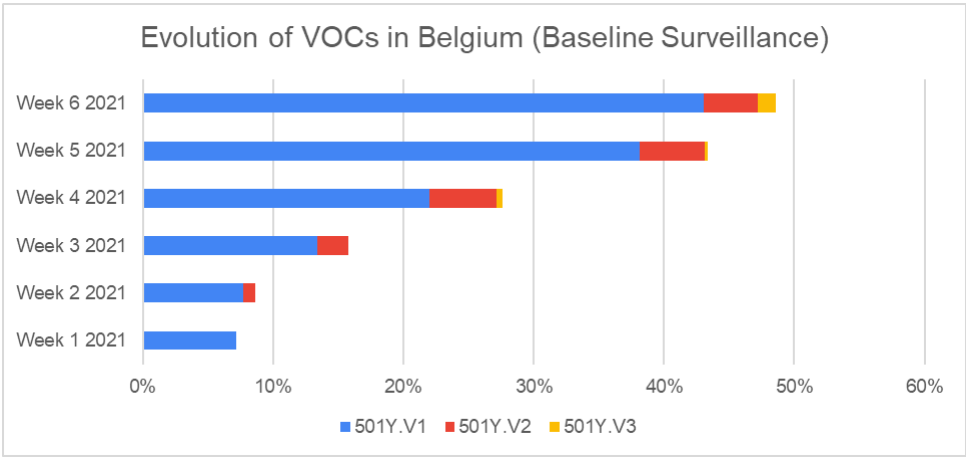

Figure 3: Proportion of VOCs identified among SARS-CoV-2 strains in Belgium through the WGS-based baseline surveillance system in place since Week 1 2021.

3. Evolution of 501Y.V1

The 501Y.V1 is currently the most prevalent VOC in Belgium. As per the baseline surveillance, it currently represents 35% of the circulating SARS-CoV-2 strains in Belgium. This estimation is confirmed by the complementary surveillance indicator based on “S dropouts”.

Since January 2021, 26.200 positive samples analysed in the 8 federal platform laboratories were reported together with the eventual presence of an “S dropout” signal, which is a reliable marker of 501Y.V1 (B.1.1.7). This indicator increased consistently since the start of the year, reaching >35% for the last two days. Modelling exercises presented in previous reports show that this VOC is expected to further increase in proportion during the coming weeks.

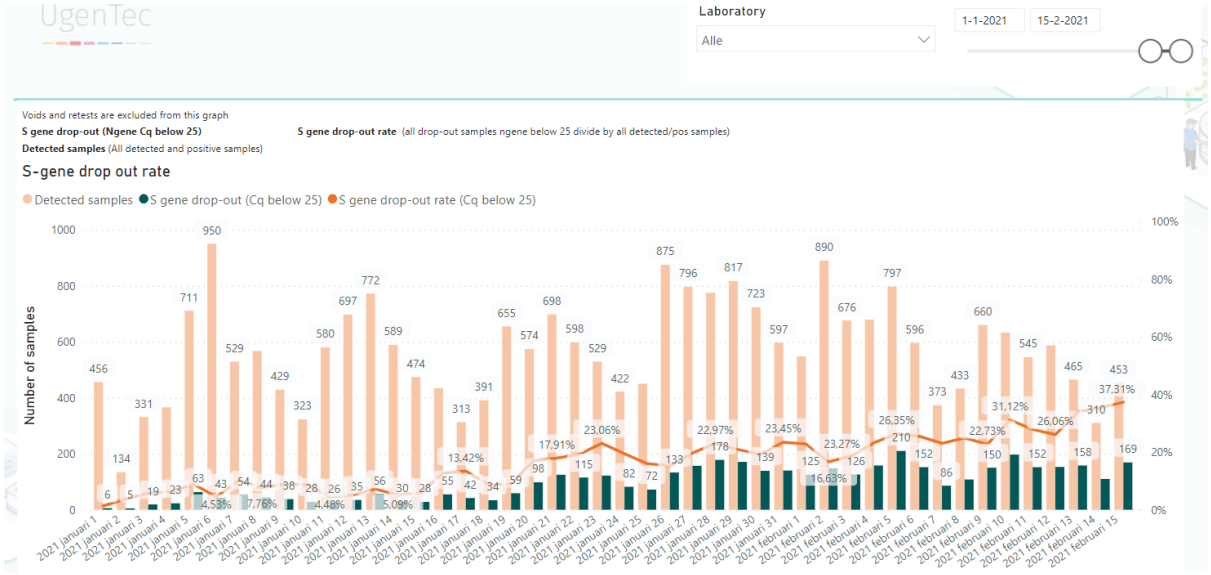

Figure 4: Evolution of the share of S dropout (orange line) in the federal platform laboratories.

4. Evolution of 501Y.V2 and 501Y.V3

The proportion of these variants among circulating SARS-CoV-2 strains is expected to further increase as a result of the combination of higher infectiousness and immune escape characteristics of these VOCs.

It is the first time that 501Y.V3 (P.1) strains (first identified in Brazil) have been reported in Belgium. It appears from the preliminary epidemiological analysis for the 4 first strains that this could be the result of at least two independent introduction events.

5. Positivity rate in the federal platform laboratories

The current positivity rate among tests performed in the 8 federal platform laboratories remained relatively stable (slight increase) over the last weeks despite the current circulation of VOCs in the country. During the last 3 days, 7-8% of the tests were reported as positive.

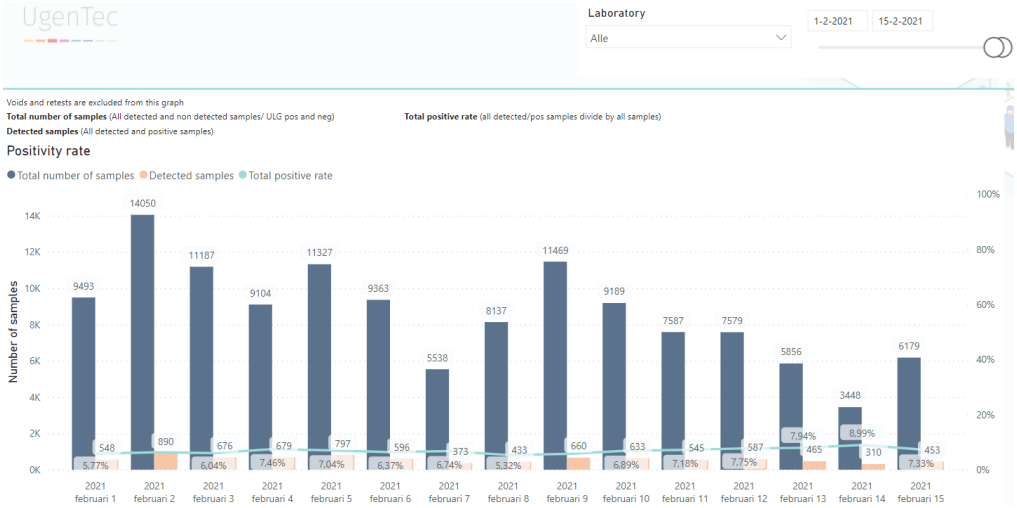

Figure 5: Positivity rate in the federal platform laboratories

6. Share of very strong positive results in the federal platform laboratories

The share of positive results with a very strong signal (Cq <15), representing patients simultaneously diagnosed during the most infectious stage of their disease, has increased over the last few weeks. Although this indicator may reflect an increasingly efficient testing strategy, it should be noted that this proportion also increased prior to the second “wave” of infections and may reflect an increase in intensity of the risk of transmission.