Genomic surveillance of SARS-CoV-2 in Belgium

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

Situation update – 18th of May 2021
(report 2021_27)

Executive summary

19.758 Belgian sequences of SARS-CoV-2 are publicly available on GISAID.

For baseline surveillance samples collected during the last two weeks (640 sequences collected between 3 May and 16 May),
- B.1.1.7 (20/501Y.V1) represented 90.3% (compared to 89.5% in the last report).
- P.1 (20J/501Y.V3) represented 5.8% (compared to 4.3% in the last report).
- B.1.351 (20H/501Y.V2) represented 0,5% (compared to 0.9% in the last report).

Other points of attention:
- 45 sequences of B.1.617.2 and 6 sequences of B.1.617.1 were deposited to date on GISAID (increasing)
- 6 sequences of B.1.1.7 with the S:E484K mutation were deposited to date on GISAID (stable)

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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. Monitoring of VoCs in Belgium

Three variants of concern (VoCs) have been introduced in Belgium around the end of the year 2020. The B.1.1.7 variant which has been introduced through numerous parallel introductions, has since then become the dominant lineage in the country and is considered as responsible for the latest epidemic resurgence ("third wave").

Over the last month, during which a representative and stable genomic surveillance could be ensured, VoCs (B.1.1.7, P.1, and B.1.351) represented respectively 83%, 8% and <3% of the sequences reported to GISAID from Belgium. The evolution of the viral population is thus relatively stable for the moment, and the constant increase of P.1 cases does not seem to accelerate.

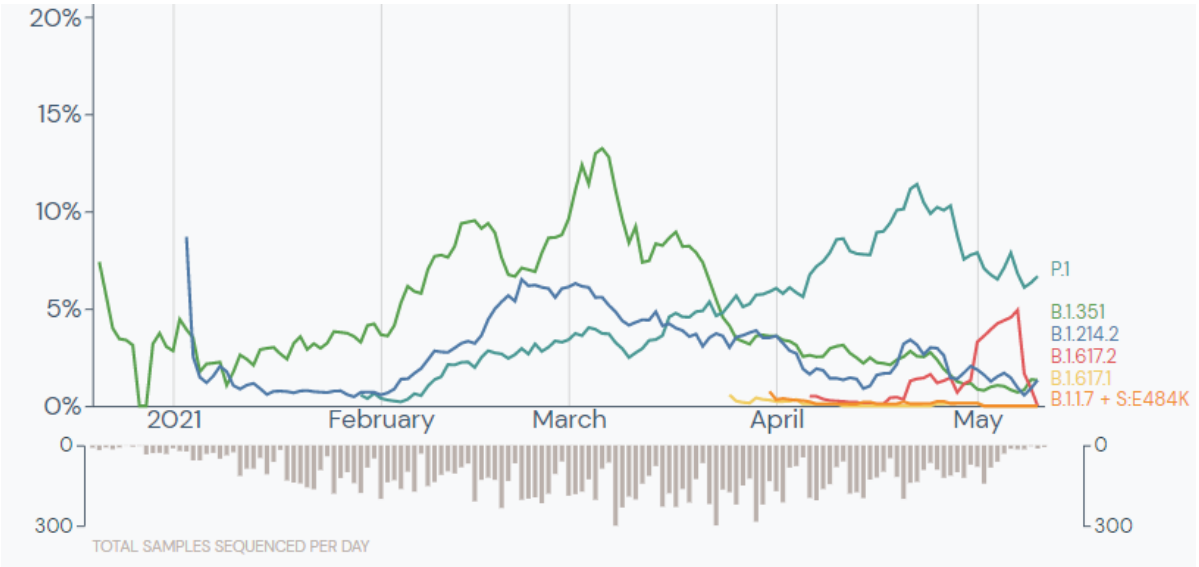

Figure 1: *Lineage prevalence over time in Belgium (combined active and baseline surveillance). B.1.1.7, P.1, B.1.351 and B.1.617.2 are currently classified as VoCs. B.1.617.1 and B.1.214.2 are among the variants of interest actively monitored in the country (source: outbreak.info & GISAID).*

<u>Particular attention to be given to B.1.617.2 (new VoC originally described in India)</u>

The increasing number of B.1.617.2 strains reported in Belgium is of concern. Although targeted active case finding interventions tend to overrepresent the current incidence of this new VOC, its high transmissibility could potentially lead to a replacement phenomenon. The cynetic of this foreseen shift cannot yet be estimated. Also, there is a current debate about its higher transmissibility being equivalent or higher than the transmissibility associated with the B.1.1.7 variant. Upcoming data and analyses should allow getting further estimates in the upcoming weeks.

A rapid viral population replacement can have important consequences on national epidemiology. Targeted interventions such as active case finding and reinforced test/trace/isolation measures can help in reducing the speed of this phenomenon and therefore mitigating it's impact. Further, continued rollout of vaccination is expected to have an important mitigation effect as it will reduce the proportion of infected people requiring medical care.
Despite some first indications of reduced neutralization, the WHO (May 10, 2021) stated that current vaccines should continue to be effective against the B.1.617.2.

List of VoCs (red) and VoIs (orange) detected in Belgium to date

Lineage	Number of Belgian cases reported on GISAID	First reported	Last reported
B.1.1.7	10619	30/11/2020	11/5/2021
B.1.351	869	20/12/2020	4/5/2021
P.1	688	29/1/2021	9/5/2021
B.1.617.2	45	6/4/2021	3/5/2021
B.1.1.7 +S:E484K	6	31/3/2021	25/4/2021
B.1.525	53	30/1/2021	22/4/2021
A.27	9	11/1/2021	20/3/2021
B.1.620	9	31/3/2021	25/4/2021
B.1.617.1	6	25/3/2021	25/4/2021
P.2	2	9/2/2021	12/2/2021
B.1.526.1	1	24/2/2021	24/2/2021
B.1.427	1	18/1/2021	18/1/2021
B.1.429	0		
B.1.526	0		
B.1.526.2	0		
B.1.617.3	0		

List of variants of concern (VoC) according to ECDC

Lineage + additional mutations	Country first detected (community)	Spike mutations of interest	Year and month first detected	Evidence for impact on transmissibility	Evidence for impact on immunity	Evidence for impact on severity	Transmission in EU/EEA
B.1.1.7	United Kingdom	N501Y, D614G	Sept 2020	Yes	Unclear	Yes	Dominating
B.1.1.7+E484K	United Kingdom	E484K, N501Y, D614G	Dec 2020	Yes	Neutralisation	Yes	Outbreaks
B.1.351	South Africa	K417N, E484K, N501Y, D614G	Sept 2020	Yes	Escape	Yes	Community
P.1	Brazil	K417T, E484K, N501Y, D614G	Dec 2020	Yes	Neutralisation	Yes	Community

List of variants of interest (VoI) according to ECDC

Lineage + additional mutations	Country first detected (community)	Spike mutations of interest	Year and month first detected	Evidence for impact on transmissibility	Evidence for impact on immunity	Evidence for impact on severity	Transmission in EU/EEA
B.1.525	Nigeria	E484K, D614G, Q677H	Dec 2020		Neutralisation		Community
B.1.427/B.1.429	USA	L452R, D614G	Sept 2020	Unclear	Neutralisation		Sporadic/Travel
P.3	The Philippines	E484K, N501Y, D614G	Jan 2021	Yes	Neutralisation		Sporadic/Travel
B.1.616	France	V482A, D614G, H655Y, G669S	Feb 2021	Detection			Single outbreak
B.1.617.1	India	L452R, E484Q, D614G	Dec 2020	Yes	Neutralisation		Outbreaks
B.1.617.2	India	L452R, T478K, D614G	Dec 2020	Yes	Neutralisation		Sporadic/Travel
B.1.617.3	India	L452R, E484Q, D614G	February 2021	Yes (m) [1]	Neutralisation		Not detected
B.1.620	Unclear (b)	S477N, E484K, D614G	Feb 2021		Neutralisation		Outbreaks
B.1.621	Colombia	R346K, E484K, N501Y, D614G	Jan 2021	Yes	Neutralisation		Sporadic/Trav

2. Evolution of variants of concern in India and the United Kingdom

India

The current epidemiological situation in India is alarming and appears to be related to the simultaneous increase of three variants of concern: B.1.617.2 (mainly), B.1.1.7 and B.1.617.1. Recently, B.1.617.2 has been categorised as a VOC by the United Kingdom.

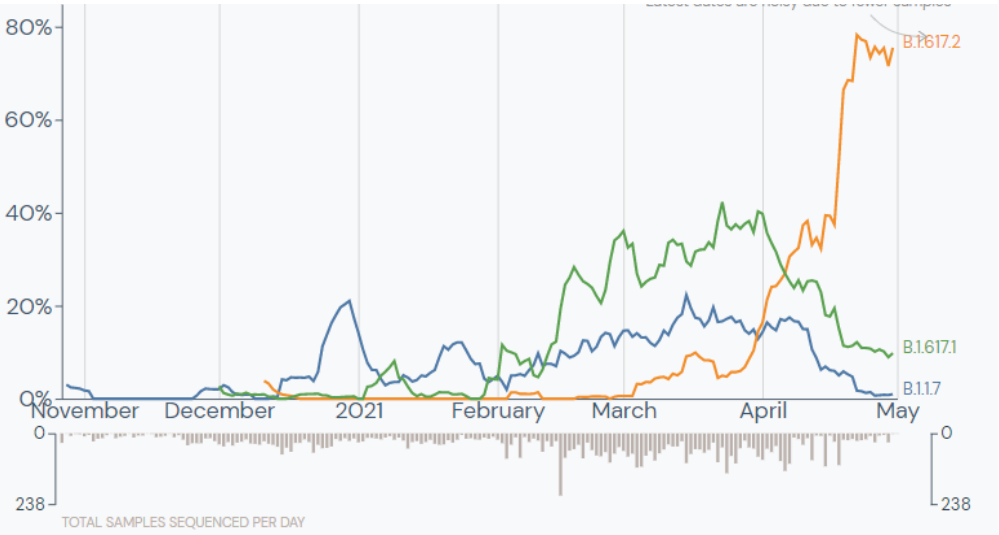

Figure 2: *Share of viral populations in India (source: outbreak.info & GISAID).*

The United Kingdom

The situation in the United Kingdom is closely monitored as this country has the most extended and strongest genomic surveillance program, and has a more advanced vaccination coverage compared to Belgium. The UK has also B.1.1.7 as dominant lineage, therefore observations from this country are relevant for the Belgian context.

In the context of a stable and low-level circulation of the virus, the UK observes a rapidly increasing number of B.1.617.2 infections. A rapid viral population shift seems to have started.

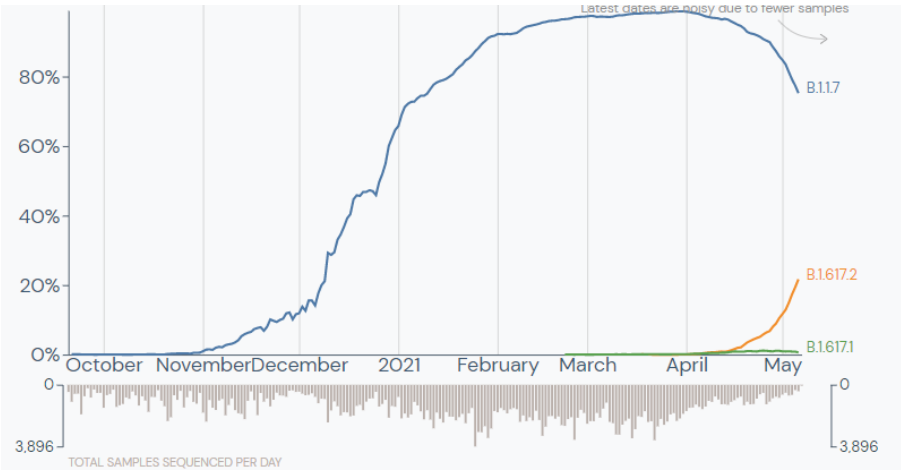

Figure 3: *Share of viral populations in the United Kingdom (source: outbreak.info & GISAID).*

3. Post-vaccination breakthrough cases

Surveillance methodology

A breakthrough infection is defined as a positive SARS-CoV-2 test at least 7 days after the full completion of a vaccination scheme (e.g. 2 doses). Samples that meet this definition are to be sent to the national reference center at UZ/KULeuven for sequencing, as agreed in the latest convention of RIZIV/INAMI.

To facilitate the transfer of samples of post-vaccination breakthrough cases to the sequencing lab in Leuven, laboratories that submit RT-PCR test results to HealthData, will receive an automatic message from HealthData notifying them that a particular sample meets the criteria of a post-vaccination breakthrough case. The linkage of positive test results to vaccination data will occur on the level of HealthData. It remains the responsibility of each lab to verify whether the sample meets the criteria for sequencing (viral load is sufficiently high, corresponding to a Ct value <25) and if so, to send the sample accompanied with the completed application form (see the website of Sciensano) to the NRC UZ/KU Leuven.

Intermediate results

The NRC is actively collecting information on post-vaccination infections. To date, 165 samples related to post-vaccination infection could be typed. All 165 samples were sampled between January 28th and May 8th, 2021.

- Vaccines involved in post-vaccination infections

  Information on the type of vaccine received is currently available for only 63 out of 165 documented post-vaccination infections. These limited numbers do not allow any conclusion, but it does not appear at this stage that specific vaccines would be particularly over- or under-represented in this group of patients.

	Share of vaccines received among fully vaccinated people	Vaccines received by patients with a post-vaccination infection	
Pfizer	86,2%	97%	
Moderna	10.3%	3%	
J&J	2.3%		
AZ	1.2%		
Total people	1.398.134	63 available to date out of 165	

Table 1: *Distribution of vaccines among post-vaccination infections.*

- Variants involved in post-vaccination infections

The distribution of lineages and variants identified in these 165 sequenced breakthrough infections is not entirely similar to the distribution of lineages and variants reported by baseline surveillance during this same period of time. These differences can be explained by immune escape mechanisms, but may also result from sampling bias or specific epidemic circumstances. These differences should therefore be interpreted with caution and will need to be further consolidated.

Variant involved	**Share in the general population during the last 3 months**	**Share among notified post-vaccination infections**	**Comment**
B.1.1.7	76%	67.3%	Not yet all post vaccination outbreaks in nursing homes included in this table
P.1	6%	8.5%	
B.1.351	5%	4.2%	Post vaccination outbreaks in nursing homes not yet included in this table
B.1.214.2	4%	7.9%	A large part (>70%) of the samples associated with a unique outbreak in a nursing home
B.1.617.1	0.5%	1.2%	
B.1.617.2	1%	1.2%	
Others	10%	9.7% ● B.1.221 (3.0%) ● B.1.160 (1.8%) ● B.1.177 (1.2%) ● B.1.214.3 (0.6%) ● Others (3.0%)	
Total sequences	9.698	165	

Table 2: *Distribution of post-vaccination infections reported to date in Belgium compared to the distribution reported for the same period of time through the baseline surveillance.*

4. Update on the variants B.1.617.1 and B.1.617.2

Currently, the majority of B.1.617.1 and B.1.617.2 (first identified in India) reported cases were detected through active surveillance (returning travellers, active case finding etc). Nevertheless, an increasing number of cases are reported through the baseline surveillance system, highlighting community transmission.

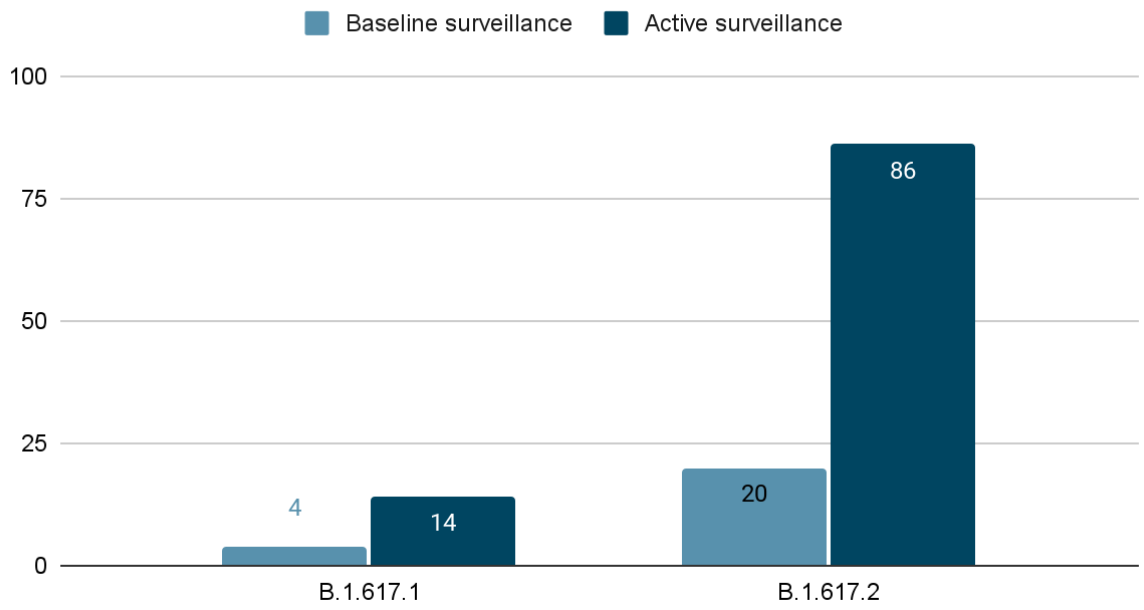

Figure 5: *Number of B.1.617.1 and B.1.617.2 cases reported between 29/3/2021 and 16/5/2021 by surveillance arm. Currently, most of these cases are found through active surveillance, but an increasing number of community transmission cases is being reported.*

Phylogenetic analysis of B.1.617.1 and B.1.617.2

Ongoing sequencing efforts have revealed an excess number of private mutations in non-Belgian genomes - illustrated by the very long branches in Figure 6 - that will have to be carefully assessed and addressed in follow-up analyses.

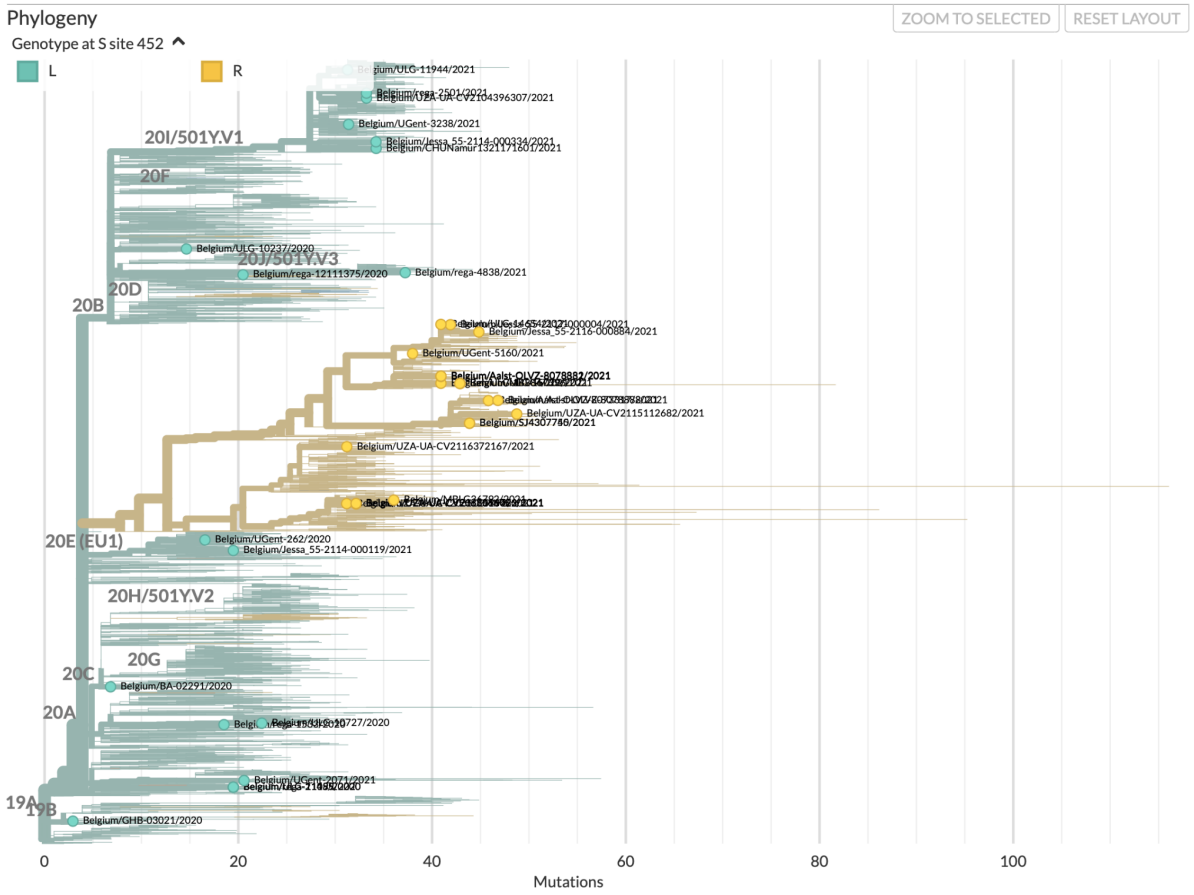

Figure 6. *Positioning of the B.1.617.1 and B.1.617.2 variants (both shown in yellow) in the global SARS-CoV-2 phylogeny. This phylogeny is highly biased as it focuses specifically on these variants.*

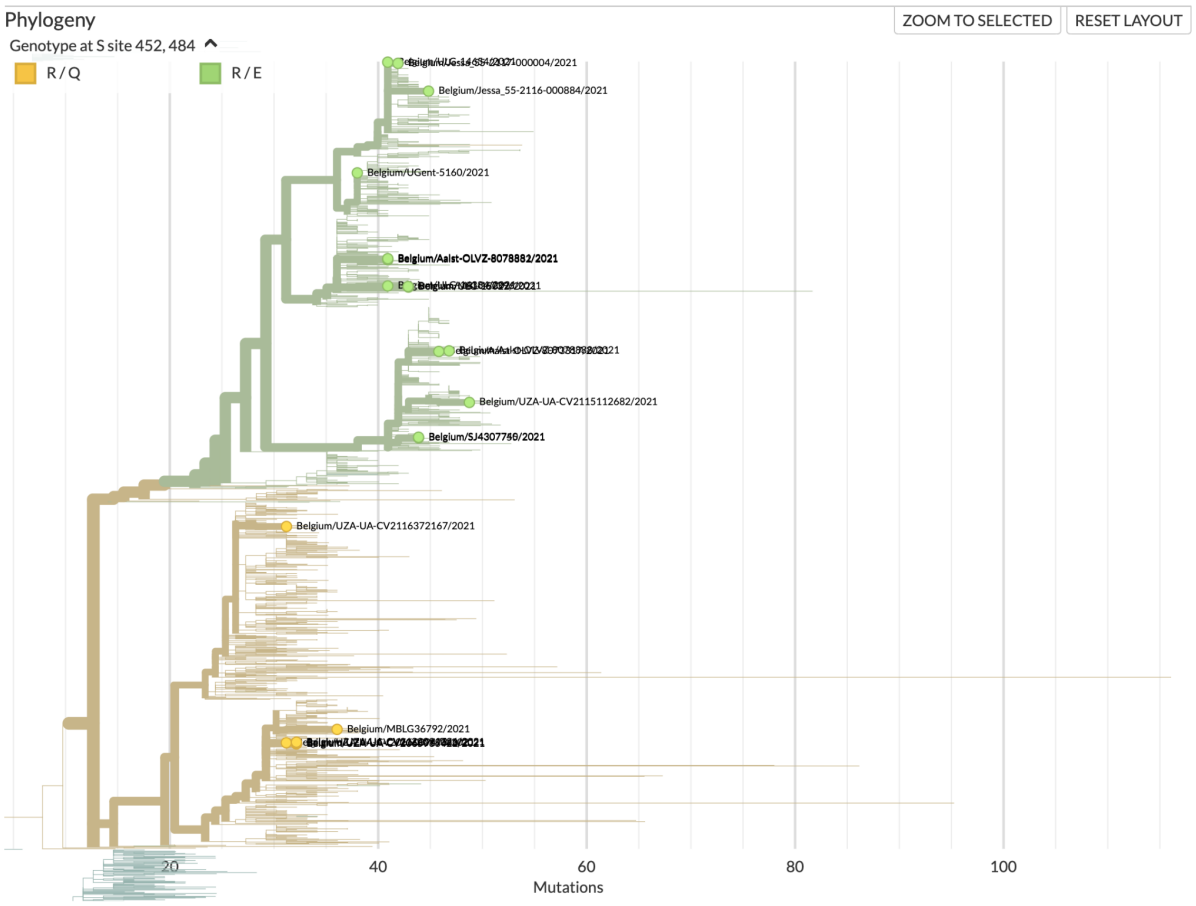

Figure 7. *Focus on the B.1.617.1 (yellow) and B.1.617.2 (green) variants. In total, 1,359 of these variant genomes from all over the world are included in this representation. The current infections in Belgium are the result of a large number of separate introductions into the country, as many of the available Belgian genomes are distinct from one another. This phylogenetic result confirms news reports of several distinct travel cases from India back to Belgium.*

Belgium mostly sees infections with B.1.617.2 and a much smaller number of infections with B.1.617.1, which is clearly visible in Figure 7. So far, B.1.617.1 infections have occurred in Schoten and the Brussels Capital Region, while B.1.617.2 infections have occurred across Belgium:

- the Brussels Capital Region
- the region in and around the city of Antwerp (Edegem, Koningshooikt, Deurne, Borsbeek)
- Aalst and Ghent
- Hasselt
- Asse
- Liège
- Knokke-Heist

Many of the available genomes on GISAID have missing location information at the moment. We will request to provide additional information for those Belgian genomes.