Hôpitaux Universitaires Genève

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Federal Office of Public Health FOPH
Public Health Directorate Communicable Diseases Division
Schwarzenburgstrasse 157
3003 Berne
Switzerland

Geneva, March 24, 2021

N/réf : LK/MS/PV

Geneva Centre for Emerging Viral Diseases

Division of Infectious Diseases

Department of Medicine

Laboratory of virology

Division of Laboratory Medicine

Diagnostic Department

SARS-CoV-2 genomic and variants surveillance in Geneva: weekly update and summary of the previous 10 weeks

The laboratory of virology of the Geneva University Hospitals as a sentinel site for the Geneva area

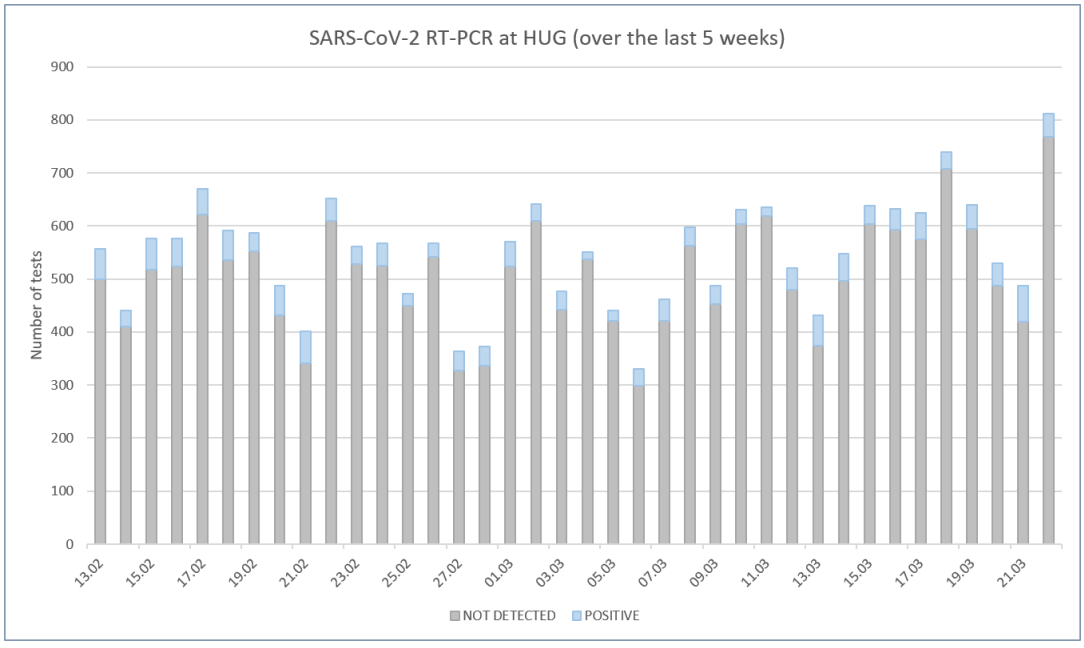
The number of tests performed at the laboratory of virology of Geneva University Hospitals represent around 1/3 of the total number of tests performed in the canton of Geneva.
Specimens analysed in our laboratory come from the community (the majority), from hospital workers (systematic screening in case of any symptoms, cluster investigations and asymptomatic HCWs as part of hospital surveillance system), from asymptomatic travellers needing a screening test, and from hospitalized patients.
All tests performed at our outpatient testing center (located in the Hospital but open to anyone from the community) are PCR-based and not Antigen-based; of course many centers in the canton are using Antigen-based tests for primary screening.
Among all SARS-CoV-2 RT-PCR-positive samples identified in our laboratory, all those with a Ct value ≤ 32 are subsequently screened for the 501Y and 484K mutations by specific RT-PCR assays. Specimens carrying the 484K mutation are subsequently tested for the 417N/T mutation.
WGS is carried out in close collaboration with the Health 2030 Genome Center in Geneva and is based on a daily random sampling of SARS-CoV-2 positive specimens by RT-PCR with as only selection criterion a Ct value ≤ 32. In some instances, sequencing can be done in specimens sent by other laboratories in Switzerland.

Current situation and summary of the recent observations:

Since the end of December 2020 and following increased genomic surveillance, “Variants of interest”, have been identified in multiple transmission events or in multiple countries. “Variants of concern” (VOCs) are additionally associated with increased transmissibility or virulence, changes in clinical disease presentation, or decreased effectiveness of public health and social measures or available diagnostics/vaccines/therapeutics. Several combined mutations define each new lineage.
Among them, B.1.1.7, first identified in the UK, has an increased risk of death compared to previous circulating viruses. There is however minimal concern of immune escape, and the different vaccines seem to have similar efficacy against this variant.
P.1, first identified in Brazil, and B.1.351 in South Africa carry the E484K mutation in addition to the 501Y mutation. Besides being more transmissible, those variants are of particular concern because of their potential to escape previous immunity. This is shown by a high reinfection rate described in regions where they are circulating, and by the decreased

efficacy of various vaccines (both approved and in development) in protecting against SARS-CoV-2 infection due to those variants. Moreover, the presence of the 484K mutation leads *in vitro* to a reduced effectiveness of some therapeutic antibody treatments and a complete loss of efficacy in combination with some other mutations.
In this regard, previous immunity due to natural infection and/or vaccination may lead to an increased selection pressure and favour the emergence and spread of variants carrying the 484K mutation. This assumption is further supported by the observation of the E484K mutation arising simultaneously in different locations (*e.g.* in New-York (B.1.526), Uganda (A.23.1), on the B.1.1.7 background in the UK).
Two weeks ago, a new French/Brittany variant was detected in Western France, belonging to the 20C/B.1 lineage. Currently, very little information is available. At the analytical level there is no concern about detection of this variant by commercially available RT-PCR tests. However, it has been suggested that it may have a different tropism, with preferential lower respiratory tract invasion, and there may be little to no virus to detect in the upper respiratory tract at the time of hospitalization. Data are currently insufficient to confirm this information.
A more detailed summary of the different variants and mutations is available among internal documents produced by the Geneva Center for Emerging Viral Diseases entitled "Variants of concern" and its updates.

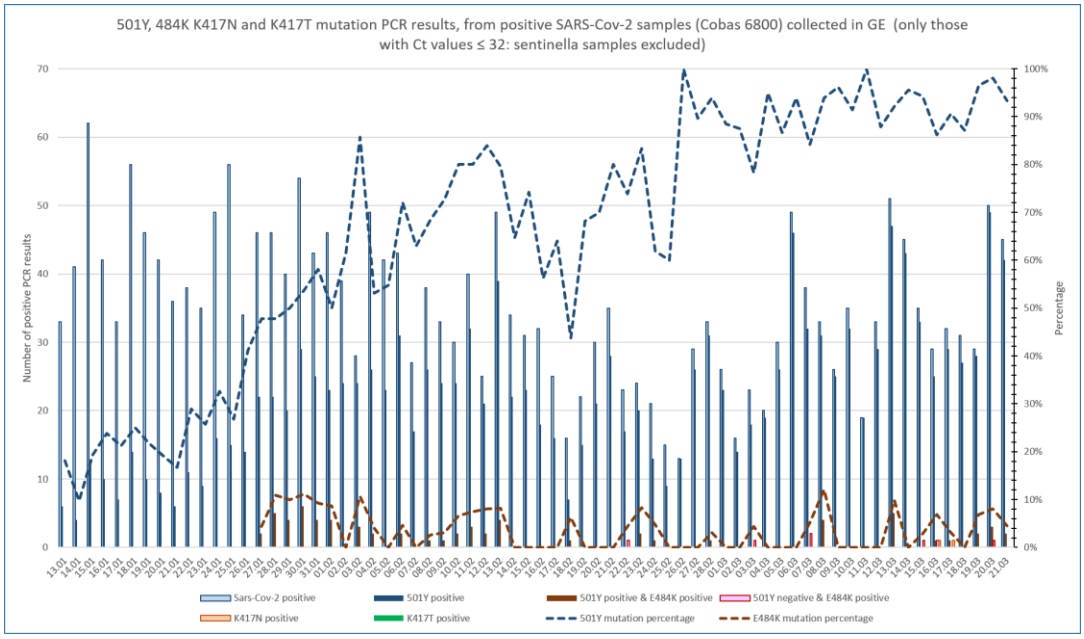
SARS-CoV-2 testing at HUG



Starting date of N501Y mutation screening: January, 5, 2021.
Starting date of E484K mutation screening: January, 27, 2021.
Starting date of 417N/T mutation screening: March 3, 2021.

There is a trend towards an increase in the number of new positive cases along with an increased number of tests performed at HUG over the last two weeks.
The screening of all specimens carrying the E484K mutation and the 417N and/or 417T mutations has been systematically reported since March 17, 2021. This additional RT-PCR test allows rapid discrimination between the P.1 and the B.1.351 variants. This aims to assist the cantonal physician team in performing contact tracing.

501Y and 484K mutation screening by RT-PCR among SARS-CoV-2 positive samples collected in GE and sent to our laboratory for primary diagnosis

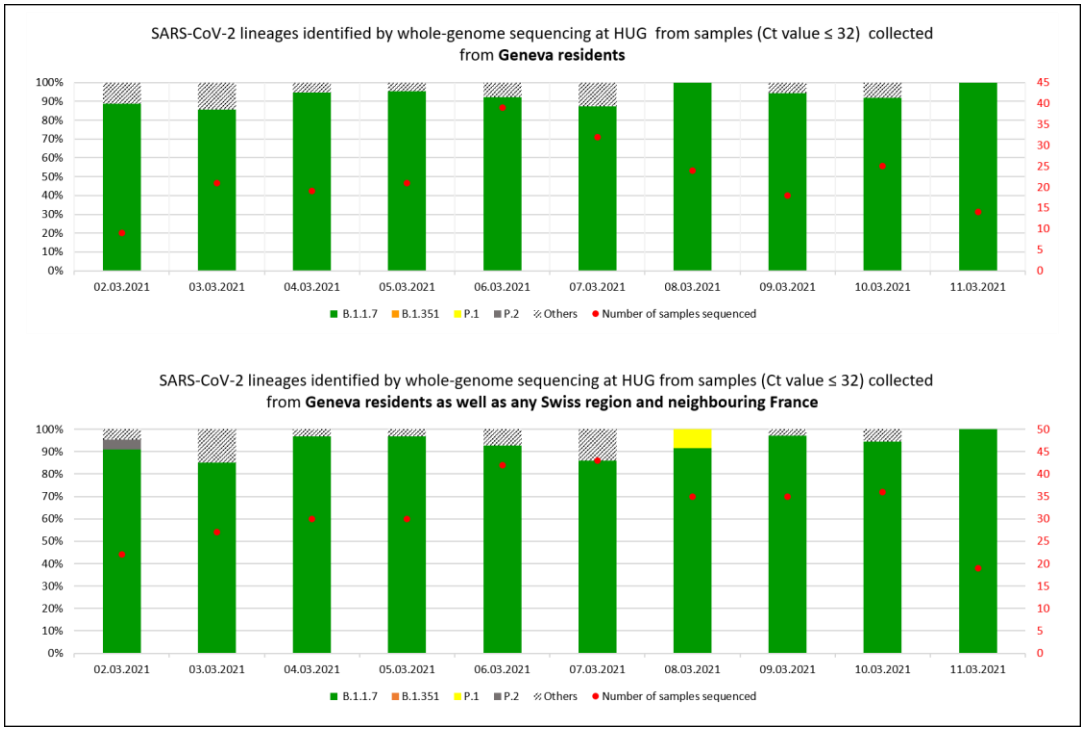


The B.1.1.7 variant carrying the 501Y mutation progressively increased in frequency over the 2 months since the beginning of the surveillance in January. Since the end of February, B.1.1.7 is causing almost all new infections in the Geneva area.

Between the end of January and mid-February, one cluster of P.1 imported through a returning traveler from Brazil, and one cluster of B.1.351 infections in a Geneva school led to an increase in 484K detection. Contact tracing intensification around those cases allowed its spread to be contained.

Since the beginning of March, a sustained low level detection of the 484K mutation has been observed. According to the Geneva cantonal physician team, these 484K-positive cases are not necessarily linked together nor do they belong to an identified cluster. This indicates that both variants are circulating at a low level in the community in Geneva. A supplementary effort is done by the Geneva cantonal physician team, which may help to contain these variants, particularly in high-risk settings, which is crucial at a time during which sufficient vaccine doses are lacking.

Most recent whole genome sequencing results performed on SARS-CoV-2 positive samples collected in GE and sent to our laboratory



This graph displays the sequences with 95% of positions covered ≥ 15x and submitted to GISAID (319 sequences obtained from samples collected from March, 2 to March 11, 2021).

Since the beginning of WGS surveillance (December 23, 2021), 2 585 sequences have been analyzed and submitted to GISAID. 1281 were B.1.1.7, 55 were B.1.351, 17 were P.1 (16 Geneva residents, 5 residents from neighboring France, 1 in Fribourg) and 4 P.2 (2 Geneva residents, and 2 from Valais).

Conclusions

Over one month, the B.1.1.7 variant rapidly became the dominant variant in the Geneva area. It is responsible of almost all new infections in the Geneva area since the end of February.
More concerning is the increase in the E484K detection in the last 2 weeks. In this regard, the screening of the 417N/T mutations assists the Geneva cantonal physician team in performing contact-tracing activities. Maintaining 484K-positive variants at low level is crucial to avoid its negative impacts.
No “Brittany” variant (Clade 20C), identified in Brittany two weeks ago in France has yet been identified in Geneva.

Laurent Kaiser **Samuel Cordey** **Manuel Schibler** **Pauline Vetter**