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Swiss national SARS-CoV-2 genomic and variants surveillance program: report of the months of March and April 2024

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1. Summary

This report covers the period of 26 February to 21 April 2024 (weeks 9-16). All data presented in this report are based on the sampling date. For an overall description of the program, please refer to previous reports or the supplementary annex.

During the months of March and April 2024, the number of positive SARS-CoV-2 tests per week remained low and even decreased from the end of February. Similarly, the test **positivity rate remained low and similar to the low rate seen at the end of February. The number of hospitalizations due to COVID-19 also remained low**. RNA levels in the wastewater remained low in March and April.

The 822 positive tests processed by laboratories participating to the program constituted over half (57.4%) of the reported positive tests in Switzerland. A total of 327 new sequences were submitted (127 collected during this period) to GISAID during the February 2024 reporting period, mainly originating from hospitalized patients.

The **JN.1** sublineage of the BA.2.86 clade **remained dominant** (>95% of wastewater sequences and >95% of clinical samples) **in March and April 2024**.

Outside of Switzerland no spread of any new highly divergent variant was detected during March nor April.

JN.1 is currently neutralized poorly following the Wu-1 & BA.5 bivalent booster. In contrast, the XBB.1.5 monovalent booster induces significant neutralization of JN.1, with JN.1 neutralization titers being roughly one third to one half of the XBB.1.5 neutralization titers. New JN.1 sublineages have been appearing, particularly KP.3, that evade antibodies raised following a JN.1 infection.

A new monoloncal antibody, pemivibart, has been validated by FDA. Data from pseudovirus and authentic virus isolates is conflicting, but live isolates displayed only a 2-fold reduction in neutralization (relative to the ancestral virus), which is overall a very good performance.

As the number of cases was low for the months of March and April, sequencing batches have been deferred. The interval between sequencing batches will likely remain long unless positive sample numbers increase again.

2. Variants of Concern (VOCs), Variants of Interest (VOI), and other surveilled variants: brief summary and special focus

The WHO currently assesses that the currently circulating VOIs are XBB.1.5, XBB.1.16, EG.5, BA.2.86, and JN.1. No variants in current circulation have been designated a Variant of Concern. All currently circulating variants are derivatives of the original "Omicron" VOC.

JN.1 and its sublineages accounted for >89% of global sequences collected in March and April 2024 (26 February to 21 April). Two spike mutations in a JN.1 background have shown clear signs of a growth advantage: F456L, and R346T. R346T was previously very common in XBB backgrounds, and was associated with immune escape. Similarly, F456L was also previously identified and was common in XBB.1.9 sublineages. As of the time of this report, R346T is present in approximately half the sequences worldwide, and F456L is present in >85% of the sequences worldwide.

No issues with detection (via PCR or antigenic tests) have been noted for any variants. Nor has increased severity has been noted. While neutralization is relatively poor against all circulating variants (due to antigenic change and immune imprinting), no major reduction similar to that seen when Omicron first appeared has been noted. Neutralization by currently available therapeutic mAbs is extremely low, but there is no loss of efficacy against other antivirals, such as protease inhibitors.

3. Epidemiology in Switzerland and number and origin of sequences produced through the program during the surveilled period

Number of cases processed by the laboratories participating in the surveillance program

From 26 February to 21 April, the FOPH reported 846 positive tests (including both RT-PCR and antigen-based tests), a substantial decrease from the 1'432 reported from 29 January to 25 February. Positive tests from the labs participating in the national surveillance program produced 86% of these (731 of 846). The percent of positives sequenced within the program remained similar: 13.1% in March and April vs 13.9% in February. The test positivity rate within the program for March and April was 5.0% compared to February's 8.0%, a substantial decrease from an already low number . Overall, the percent of sequenced ascertained positive cases was 11.3%, an increase from February.

Although case ascertainment rates may be low, there had been continuing trend since late November/early December 2023 towards decreases in the number of cases, hospitalizations, and RNA levels in wastewater. As of the time of this report, there has been a slight increase in RNA wastewater levels (in May) For more information, please refer to the BAG dashboard (https://idd.bag.admin.ch/). Detailed data regarding the total number of tests performed each week by the laboratories participating in the surveillance program are available in supplementary Table 1.

Number of declared SARS-CoV-2 sequences produced through the surveillance program

A total of 96 SARS-CoV-2 sequences have been declared to have been processed during this period. There are 126 sequences available on GISAID that were submitted during this period (and 67 collected during this period) as of 6 June 2024.

Week	Date	Number of sequences declared and successfully submitted to GISAID, January 2024
9	Feb. 26 to March. 3	43
10	Mar 4 to Mar 10	
11	Mar 11 to Mar17	19
12	Mar 18 to Mar 24	
13	Mar 25 to Mar 31st	30
14	April 1st to April 7	
15	April 8 to April 14	4
16	April 15 to April 21	
	Total	96

Table 1: number of sequences submitted to GISAID through the surveillance program. Note these data are not by sampling date but rather by submission to GISAID date. For a breakdown by laboratory, see the appendix.

Sequencing in Switzerland by the national SARS-CoV-2 surveillance program

Numbers of SARS-CoV-2 sequences submitted and positive tests each week continued to decrease during the March and April 2024 reporting period (weeks 9-16).

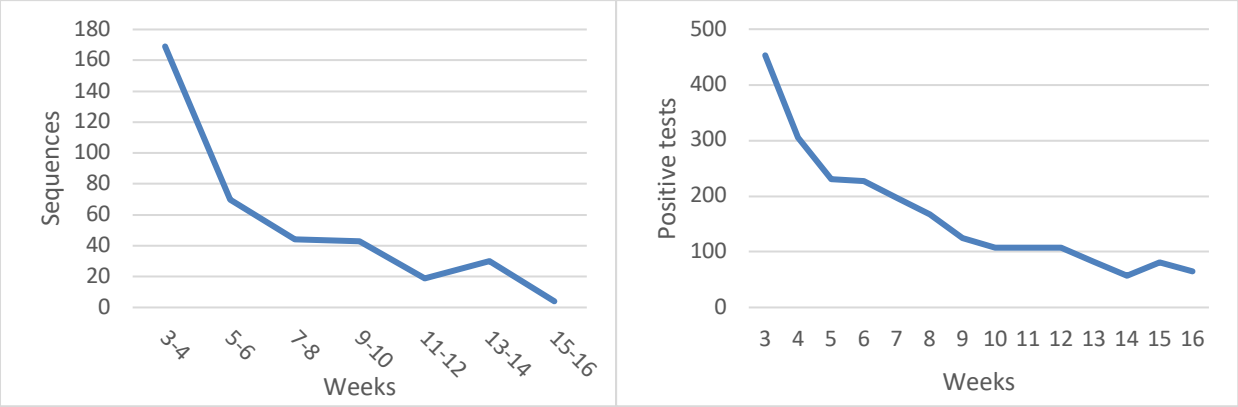

Figure 1: Sequences submitted and positive tests from all regions of the program for 2024, note the continuos but slower decline since weeks 5 to 6

Recently circulating variants in Switzerland

The vast majority of circulating viruses are JN.1 sublineages now. During the November 2023 reporting period, the XBB.1.9 sublineage lost its dominance as the BA.2.86 sublineage JN.1 rose significantly, and it is still dominant as of the time of this report. Overall, 1 XBB sequence (EG.5.1 sublineage HK.3.2) was detected during this period, accounting for 1.5% of the total sequences, in contrast there were 65 BA.2.86 sequences (64 were JN.1*) accounting for 98.5% of March and April's sequences. No other variant had substantial circulation. For more details, see: https://cov-spectrum.ethz.ch/explore/Switzerland.

Region	BA.2.86*	JN.1*	XBB*	others	Recombinant	Sequences
All	1 (1.5%)	63 (97%)	1 (1.5%)	0	0	65

Table 2: number of sequences corresponding to selected variants in Switzerland from 26 February to 21 April, according to data received by 6 June 2024.

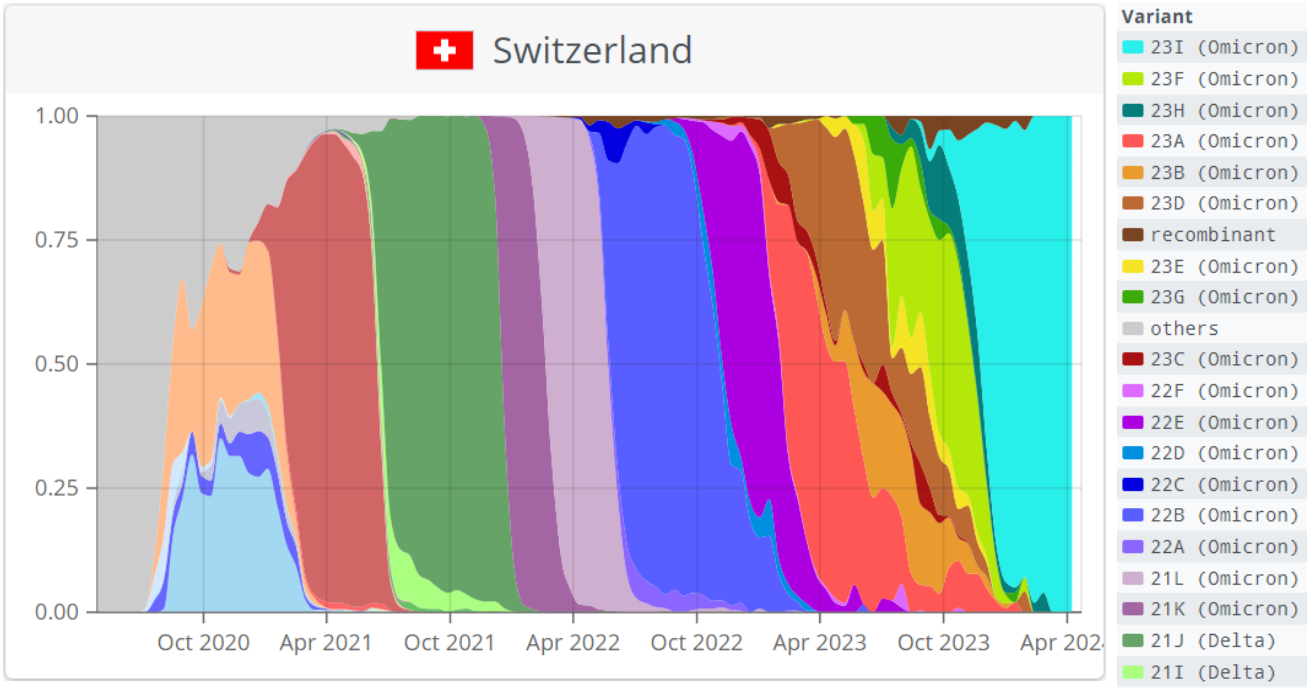

Figure 2: proportion of Swiss sequences over time by variant. For more information, see: https://covariants.org/per-country. Note: 21 J- B.1.617.2 (Delta); 21K- BA.1; 21L- BA.2; 22B- BA.5; 23A- XBB.1.5 (red); and 23I- BA.2.86 (cyan). Also note that the 23I (BA.2.86) includes the JN.1 subvariant

4. Surveillance of mutations associated with reduced available treatment efficacy

Resistance mutations to available antivirals

AA position	World	Europe	Switzerland
Paxlovid®	(Nsp5 mutations)		
15	0.01 (5)	0	0
48	0.04	0	0
49	0.02	0	0
140	0.01 (4)	0	0
143	0.01 (4)	0	0
144	0.01 (5)	0	0
165	0.01 (3)	0	0
166	0.01 (4)	0	0
167	0.01 (3)	0	0
168	0.01 (3)	0	0
172	0.01 (3)	0	0
173	0.01 (6)	0	0
186	0.01 (7)	0.01 (1)	0
188	0.02 (9)	0	0
189	0.02 (9)	0	0
192	0.02 (8)	0	0
194	0.03	0	0
248	0.00 (1)	0	0
252	0.00 (2)	0	0
304	0.01 (3)	0	0

Current data suggests that all monoclonal antibodies commercially available in Switzerland, such as sotrovimab, are unable to effectively neutralize JN.1 and its subvariants. The mAb Pemivibart, newly approved by the FDA, currently neutralizes JN.1 with only a 2-fold decrease relative to the ancestral virus, which is very good performance. Escape mutations to Pemivibart have not been evaluated in sufficient detail to follow.

Paxlovid remains effective against all circulating variants, and escape mutations remained rare in Switzerland and worldwide (all less than 0.05%) in March and April 2024 (Table 3), with Nsp5:48 mutations being the most common worldwide (0.04%). In March and April, only one sequence with a mutation at a known Paxlovid resistance site (Nsp5:186) was detected in Europe, and none were detected in Switzerland.

Table 3: Frequency (%) of mutations at residues linked (by deep mutations scanning or other experimental results) to escape from Paxlovid® (5-fold cutoff), March and April 2024 (according to data as of 6 June, 2024). Numbers in parentheses denote the total number of sequences detected with a given mutation when it is ≤10.

Acknowledgements:

https://bsse.ethz.ch/cevo/research/sars-cov-2/swiss-sars-cov-2-sequencing-consortium.html

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Appendix:

SARS-CoV-2 epidemiology in Switzerland:
We used publicly available data on COVID-19 as reported by FOPH (https://idd.bag.admin.ch/) and sequence data submitted to GISAID to provide a summary of the SARS-CoV-2 epidemiology in Switzerland.

week	date	Total PCR tests	Positive tests	Sequenced	% positives sequenced
9	Feb. 26 to March. 3	2'179	125	43	18.5
10	Mar 4 to Mar 10	2'090	107		
11	Mar 11 to Mar17	1'993	107	19	8.9
12	Mar 18 to Mar 24	1'882	107		
13	Mar 25 to Mar 31st	1'720	82	30	21.6
14	April 1st to April 7	1'628	57		
15	April 8 to April 14	1'557	81	4	2.7
16	April 15 to April 21	1'437	65		
	Total	14'486	731	96	13.1

Supplementary Table 1: Total number of tests performed by the laboratories participating in the surveillance program from 26 February to 21 April, 2024.

week	Date	HUG	CHUV	ICH-VS	IFIK	UZH IMV	USB	EOC	All
9	Feb. 26 to March. 3	10	11	10	0	7	3	2	43
10	Mar 4 to Mar 10								
11	Mar 11 to Mar17	6	10	3	0	0	0	0	
12	Mar 18 to Mar 24								
13	Mar 25 to Mar 31st		4	12	0	0	0	0	
14	April 1st to April 7	11	3		0		0		
15	April 8 to April 14	0	2		2	0	0	0	
16	April 15 to April 21		0		0		0		
	Total	27	30	25	2	7	3	2	96

Supplementary Table 2: number of sequences submitted to GISAID by each laboratory during the surveilled period (from 26 February to 21 April, 2024). Note the dates of the sequencing blocks differ significantly between centers, primarily due to low sample numbers.