Characterization of SARS-CoV-2 ORF6 deletion variants detected in a nosocomial cluster during routine genomic surveillance, Lyon, France

Running title: SARS-CoV-2 ORF6 deletion variant detected in COVID-19 cluster

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Abstract (250 word maximum)

Through routine genomic surveillance of the novel SARS-CoV-2 virus (n=229 whole genome sequences), 2 different frameshifting deletions were newly detected in the open reading frame (ORF) 6, starting at the same position (27267). While the 26-nucleotide deletion variant was only found in one sample in March 2020, the 34-nucleotide deletion variant was found within a single geriatric hospital unit in 5/9 patients sequenced and one health care worker with samples collected between April 2nd and 9th, 2020. Both the presence of the 34-nucleotide deletion variant limited to this unit and the clustering of the corresponding whole genome sequences by phylogeny analysis strongly suggested a nosocomial transmission between patients. Interestingly, prolonged viral excretion of the 34-nucleotide deletion variant was identified in a stool sample 14 days after initial diagnosis for one patient. Clinical data revealed no significant difference in disease severity between patients harboring the wild-type or the 34-nucleotide deletion variants. The *in vitro* infection of the two deletion variants on primate endothelial kidney cells (BGM) and human lung adenocarcinoma cells (Calu-3) yielded comparable replication kinetics with the wild-type strain. Furthermore, high viral loads were found *in vivo* regardless of the presence or absence of the ORF6 deletion. Our study highlights the transmission and replication capacity of two newly described deletion variants in the same ORF6 region.

Importance (150 word maximum)

While the SARS-CoV-2 genome has remained relatively stable since its emergence in the human population, genomic deletions are an evolutionary pattern previously described for the related SARS-CoV. Real-time genomic monitoring of the circulating variants is paramount to detect strain prevalence and transmission dynamics. Given the role of ORF6 in interferon modulation, further characterization, such as mechanistic interactions and interferon monitoring in patients, is crucial in understanding the viral-host factors driving disease evolution.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic triggered by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has continued to spread globally since its emergence in China in late 2019 (1, 2). Countries and localities have implemented various levels of public health mitigation measures with debatable success in an effort to control virus propagation (3–6). The challenge in better understanding the fundamental characteristics of this novel virus includes the heterogeneous disease reports in conjunction with no clear treatments or vaccines yet available or approved (7–9). Epidemiological tracking is paramount in the context of this current pandemic (10, 11). In particular, the genomic surveillance of circulating virus variants, such as with the seasonal epidemics of the influenza virus or even with the 2003 SARS epidemic, has brought useful information in understanding their respective evolutionary dynamics (12, 13). Recent tracking reports have discussed the high frequency and global distribution of a variant harboring the D614G substitution located on the SARS-CoV-2 spike protein. While higher infectious titer and increased protein stability have been associated with this variant, a clear fitness advantage has not been unequivocally established (14, 15). Historically, evolution of the related SARS-CoV virus is defined by deletion regions that impact the open-reading frames (ORF) of its genome (16, 17). Several deletions of large variations in size and prevalence have already been described in the SARS-CoV-2 genome (18–20).

The aim of this study was to therefore describe clinical patient data and the viral replication capacity of two newly detected ORF6 deletion variants detected in early April from routine genomic surveillance of COVID-19 patients in Lyon, France.

Results

ORF6 Deletion Variants Detected During Routine Genomic Surveillance

As part of the Auvergne-Rhône-Alpes (ARA) regional surveillance, 229 samples collected between Feb 2nd and April 12th were sequenced by the French National Reference Center of Respiratory Viruses. These samples originated mainly from the Hospices Civils de Lyon (HCL) (149 sequences from 58 units within 11 different hospital sites), with some from other hospitals in the Lyon area (24 sequences) and other regional hospitals (56 sequences, 12 cities).

Of these 229 samples, 6 sequences were shown to carry a 34-nt deletion (at position 27267-27300), henceforth denoted as D34, and 1 sequence a 26-nt deletion (at position 27267-27292), denoted as D26 (Figure 1). These deletions are both frameshifting deletions in the ORF6, starting at the same 27267 position after a stretch of 3 T at 27264-27266 (Figure 2). Because of the frameshifting, the D34 variant generates a premature stop codon (at position 27308, Wuhan-Hu-1 numbering), resulting in a presumed truncated 24 amino acid protein, instead of 61 in the wild-type (Wuhan-Hu-1 and all other sequences described yet). The D26 variant yields a 28 amino acid protein with its premature stop codon at position 27312 (Wuhan-Hu-1 numbering) (Figure 2). These deletions have not yet been described on the CoV-GLUE resource, which lists all genomic variants in SARS-CoV-2 sequences available on the GISAID database (Supplementary Data 1). Of note, ORF6 variants are annotated at different positions in CoV-GLUE to maximize amino acid alignment.

The 7 sequences carrying an ORF6 deletion belong to lineage B1, a lineage widely circulating in Europe (Supplementary Data 1). There were between 0 and 3 SNP (Single Nucleotide Polymorphism) differences among D34 strains, for which 3/6 mutants displayed 1 to 3 SNPs, and between 2 and 4 SNPs between D26 and D34 strains (Supplementary Data 2).

Evidence for direct transmission of the ORF6 34-nt deletion variant

The D34 samples were all collected from hospitalized patients or health care workers (HCW) in the same geriatric rehabilitation unit in the Hospices Civils de Lyon (GRU-3), between April 2nd and April 9th, while the sample with the 26-nt deletion was collected one month earlier (March 10th) in a geriatric unit of another hospital (Table 1). The hospitals are 80 km apart and there was no evidence for the transfer of patient #73 with the 26-nt deletion into GRU-3. To track the origin of the deletion, all patients hospitalized in the GRU-3 geriatric unit and all samples collected between March 18th and April 9th with high viral loads of SARS-CoV-2 (RT-PCR Ct value <20) were sequenced (n=9). In total, 44% (4/9 patients) were infected with the WT SARS-CoV-2 ORF6 (samples collected between March 18th -30th), with no read carrying the deletion at a minor frequency. Out of the 4 WT SARS-CoV-2 ORF6, three sequences were very similar to D34 and carried a G27289T SNP (D30Y), which has already been identified in three patients from England between April 20th and 27th, 2020 (Figure 1). The other 55% (5/9 patients), in addition to 1 HCW, were infected with the 34-nt deletion (samples collected after April 2nd) with 100% of the reads carrying the deletion for each patient. Overall, 8/9

sequences of GRU-3, corresponding to those of the D34 variants and those of the three WT strains carrying the ORF6 G27289T SNP were clustered together, while the sequence of the patient #38 was more divergent. We could not investigate whether the mutation spread after April 9th as only one COVID-19 patient was hospitalized in this geriatric unit since, for which their viral load (Ct>30) was too low for mNGS.

34-nt ORF6 deletion variants yielded similar clinical presentations as WT ORF6 in hospitalized patients

Clinical data were studied on hospitalized patients in GRU-3 (i.e. excluding the HCW #63 to better control for confounding variables (e.g. age and comorbidities)) to compare COVID-19 severity between patients infected with D34 and with WT SARS-CoV-2 (n=9) (Table 1). The median age of hospitalized patients was 87 years (ranging from 78 - 97), with 7 patients presenting at least cardiovascular disease as a risk factor (Table 1). Other comorbidities included hypertension (n=5), obesity (n=1), and chronic obstructive pulmonary disease (n=1).

Clinical presentations of hospitalized patients with the D34 variants (n=5) were classified as asymptomatic for one patient, upper respiratory tract infection for 2 patients, and lower respiratory tract infection (pneumonia) for 3 patients. To evaluate disease severity in relation to the D34 deletion, mild (asymptomatic and URTI, n=5) versus severe COVID-19 (LRTI, n=4) was compared by Fisher's exact test. No significant difference in clinical presentation could be observed between hospitalized patients harboring or not the ORF6 deletion (p>0.99).

From the five hospitalized patients harboring D34 deletion, 2 died from COVID-19 infection, all presenting LRTI and comorbidities. One patient (#25) died at day 5 after diagnosis, but their death was not related to COVID-19 infection but to septicemia. To evaluate disease outcome in relation to the D34 deletion, death from COVID-19 versus favorable outcome (including non-COVID-19 death) was compared by Fisher's exact test. No significant difference in disease outcome could be observed between hospitalized patients harboring or not the D34 deletion (p=0.44).

Notably, patient #47 harboring a D34 variant was still positive after 14 days in respiratory and stool samples. Virus present in the stool was 100% identical to the first virus sequenced from respiratory samples. Unfortunately, the respiratory sample at day 14 could not be sequenced due to Ct >30.

137 **SARS-CoV-2 deletion variants yield comparable replication kinetics to reference strain**

138 Two genomes representative of ORF6 deletion variants found in this regional circulation were
139 selected for replication tests: hCoV-19/France/ARA22647/2020 (D34 variant) and hCoV-
140 19/France/ARA0731/2020 (D26 variant). These genomes were compared against the reference
141 genome hCoV-19/France/ARA24023/2020 (devoid of any deletions), which was the most similar
142 isolated strain sequenced available in the laboratory at the time of the investigation. The reference
143 genome had 1 to 3 SNPs compared with D26 and D34 variants (Supplementary Data 2).

144 Replication kinetics measured by viral genome quantification revealed no significant difference
145 between the three strains throughout the course of *in vitro* infection on both BGM and Calu-3 cell lines
146 (Figure 3). However, a significant difference was observed between cell lines for each strain, with an
147 increased level of replication on BGM (as early as 24 hours post-inoculation). More specifically, viral
148 replication spiked rapidly on BGM cells within the first 48 hours, before reaching a plateau at 72
149 hours. Conversely, viral replication on Calu-3 cells rose steadily within the first 48 hours, before
150 reaching a plateau at 96 hours. Of interest, a 2-log difference was observed for maximum genome
151 quantification between BGM and Calu-3, with an average of 5.76×10^{12} and 4.01×10^{10} copies/mL,
152 respectively.

153

154 **Discussion**

155 Despite reports of the relative stability of the SARS-CoV-2 genome within the human population,
156 whole genome sequencing has revealed recurrent variants with variable mutation patterns over the
157 course of the pandemic and within distinct geographic regions (10, 18, 21, 22). Here we describe
158 clinical data and the viral replication ability associated with large ORF6 deletion variants identified
159 through surveillance of patients from the same hospital unit. The CoV-GLUE phylogenetic resource
160 revealed no other international sequence harboring the ORF6 deletions described herein. However,
161 other reports of similar patterns of genomic deletions in the SARS-CoV-2 genome since its
162 emergence have already been described, including in the ORFs 6, 7 and 8 (19, 20, 22, 23).

163 The origin of the D34 deletion is still unknown. However, as the WT virus isolated from GRU-3
164 patients were genetically close to the D34 variants, the GRU-3 patients infected by the WT virus in

March could have been the initial source of the D34 deletion. Nevertheless, its introduction since April 2nd with its limited presence in the hospital unit thereafter and the clustering of the corresponding whole genome sequences by phylogeny analysis strongly suggest a nosocomial transmission of the D34 variant. Importantly, the persistence of the same D34 consensus sequence in a patient's stool sample 14 days after diagnosis from a nasopharyngeal sample gives emphasis to the enteric tropism capacity of D34 variants and the potential contribution to nosocomial transmission (24). None of the GRU-3 patients with WT or deletion strains presented any intra-host diversity in the ORF6 deletion region that would have been indicative of a recent mutation or recombination.

The similar consensus sequences in the nasopharyngeal and in the stool samples over a 2-week period suggest an apparent low intra-host evolution. However, different sites of SARS-CoV-2 replication might have a different impact on the intra-host evolution, but we could not provide the consensus sequence from the nasopharyngeal sample collected at day 14 due to low viral load to confirm this hypothesis (25). Moreover, the normal rate of mutation of SARS-CoV-2 has been reported at about 2.5 mutations per month (26, 27). Nevertheless, the fact that D34 variants had 1 to 3 SNP differences between consensus sequences of D34 strains collected between one week might highlight a higher mutation rate than normal and be linked to adaptative mutations following the deletion. Evidence of adaptation by means of genomic deletions during the middle and late phases of the SARS-CoV 2003 epidemic has been tenuously described (16, 17, 28–30). Our restrictive number of sequenced strains to date does not currently allow conclusive population prevalence information for the Auvergne-Rhône-Alpes region. The importance of such genomic variants by NGS investigation during the evolution of disease transmission and population prevalence should not be overlooked (13, 31, 32). Further genomic surveillance is needed to assess specific evolutionary patterns of these variants.

Our study characterized the D34 and D26 ORF6 variants, showing no significant impact on replication *in vitro* in comparison to a wild-type strain, in two different cell lineages. The comparable replication kinetics between wild-type and deletion strains determined *in vitro* and *in vivo* replication capacity (the latter being assessed by RT-PCR from diagnosis, Ct<20) is supported by the congruent in vivo replication capacity (the latter being assessed by RT-PCR from diagnosis, Ct<20). Furthermore, there was no significant difference in disease severity between patients at the GRU-3 hospital unit

194 harboring D34 ORF6 variant or WT. It is important to note that interferon immunoprofiling of patients,
195 a key factor in disease manifestation, was not assessed and remains to be explored (33).

196 Research on the SARS-CoV ORF6 has attributed this accessory protein with potential functions of
197 intracellular membrane rearrangements, of interferon induction inhibition, and of replication
198 stimulation (34–36). Recent literature confirms the interferon signaling inhibitory function of the SARS-
199 CoV-2 ORF6 protein (37). Another recent study reported a 27-nt in-frame ORF6 deletion (at position
200 27264 - 27290) and demonstrated important three-dimensional structural alterations to the protein
201 (23). Whereas this in-frame deletion variant would have emerged during passaging on VeroE6 cells,
202 the D34 and D26 variants already presented these deletions in the initial clinical isolates before cell
203 culture. Frameshift modifications, especially the -1 programmed ribosomal frameshift allowing ORF1b
204 translation, have been known to alter coronavirus genomic and subgenomic RNA production
205 efficiencies (38–41). And so, we can postulate that ORF6-mediated frameshifts can affect
206 downstream elements, such as the critically multifunctional nucleocapsid (N) protein (42, 43). Further
207 genomic and structural investigations are needed to explore the impact of these ORF6 deletions, in
208 terms of ribosomal frameshift stimulators and RNA translation production ratios, as well as innate host
209 immunity modulation. The integration of more fundamental research dedicated to elucidating the
210 factors that impact SARS-CoV-2 replication, transmission, and disease progression will ultimately
211 help translational projects to advance the fight against the current COVID-19 pandemic.

212

213 **Material and Methods**

214 **Sequencing**

215 Early routine genomic surveillance of SARS-CoV-2 in the National Reference Center (NRC) of
216 Respiratory Viruses is based on daily random selection of samples with SARS-CoV-2 detected with
217 quantitative reverse-transcriptase polymerase chain reaction (qRT-PCR) cycle threshold (Ct) <20 (6),
218 which were then sequenced using an RNA metagenomic next-generation sequencing (mNGS)
219 method previously described (18). Briefly, viral genetic material contained in nasopharyngeal and
220 stool samples was extracted by the EMAG® platform (bioMerieux, Lyon, FR). After DNAse treatment
221 (Life Technologies, Carlsbad, CA, USA), samples underwent random amplification using Whole
222 Transcriptome Amplification (WTA2 kit, Sigma-Aldrich, Darmstadt, DE) before sequencing on an

Illumina NextSeqTM 550 with mid-output 2x150 flow cell. Importantly, the strains displaying an ORF6 deletion were confirmed by 3 other techniques, including capture- and amplicon-based strategies (44). Sequencing of patient samples began on Feb 8th and is ongoing. For the stool sample, an amplicon-based approach developed by the ARTIC network (https://artic.network/ncov-2019) combined with Oxford Nanopore Technologies sequencing was used.

Phylogeny

Multiple sequence alignment was performed using the DECIPHER package in R (45). Pairwise distances were computed using the Kimura (K80) model implemented in the function dist.dna, deleting the sites with missing data in a pairwise way. The phylogenetic tree was constructed using R software using ape package and the neighbor joining evolutionary method (hCoV19/Wuhan/IPBCAMSWH01/2019 as the root). CoV-GLUE resource [http://cov-glue.cvr.gla.ac.uk, (46)] was used to generate phylogenetic placement of the mutants, annotate the sequences, and check the prevalence of the deletions among worldwide sequences. Codon numbering is based on the Wuhan-Hu-1 sequence.

Virus replication kinetics

Replication kinetics was performed on both confluent buffalo green monkey (BGM) (BioWhittaker Europe) and human lung adenocarcinoma (Calu-3) cells (ATCC® HTB-55™, Plateforme iPS, NeuroMyoGene Institute, Lyon, FR) at a multiplicity of infection (MOI) of 10^{-3} at 37°C for 7 days, fully respecting the WHO interim biosafety guidance related to the coronavirus disease (47). Comparative viral particle quantification of culture supernatant was performed by RdRp Institut Pasteur qRT-PCR on a QuantStudio™ 5 System (Applied Biosystems, ThermoFischer Scientific) with a standard curve after semi-automated EMAG® extraction (bioMérieux, Lyon, FR) (6). Statistical analysis was performed by two-way ANOVA with Tukey multiple comparisons between both factors of comparison (virus strain and cell line) on GraphPad Prism (software version 8.4.3).

Ethics

Samples used in this study were collected as part of an approved ongoing surveillance conducted by the National Reference Center for Respiratory Viruses (NRC) in France (WHO reference laboratory providing confirmatory testing for COVID-19). The investigations were carried out in accordance with

the General Data Protection Regulation (Regulation (EU) 2016/679 and Directive 95/46/EC) and the French data protection law (Law 78–17 on 06/01/1978 and Décret 2019–536 on 29/05/2019). Samples were collected for regular clinical management during hospital stay, with no additional samples for the purpose of this study. Patients were informed of the research and their non-objection approval was confirmed. This study was presented by the ethics committee of the Hospices Civils de Lyon (HCL), Lyon, France and registered on the HCL database of RIPHN studies (AGORA N°41).

Data availability

The SARS-CoV-2 genomes sequenced in this study were deposited on the GISAID database (https://www.gisaid.org/) on a regular basis, accession numbers can be found in Supplementary Table 1.

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Competing Interests

The authors declare no competing interests.

BL is a member of the French Scientific Committee for SARS-CoV-2.

Figure legends

FIGURE 1. Phylogenetic tree of SARS-CoV-2 full genome sequences from ARA patients (n=229). The phylogenetic tree was constructed using R software using ape package and the neighbor joining evolutionary method (hCoV19/Wuhan/IPBCAMSWH01/2019 as the root). The colored branches denote the hospital unit origin of the sequence and ORF6 status. On the right, multiple sequence alignment from nucleotide position 27267-27303 (Wuhan-Hu-1 numbering) is illustrated, with the 26-nt and 34-nt deletions depicted in black. The deletion sites of interest were not included for genetic distance calculation.

FIGURE 2. SARS-CoV-2 genome map at ORF6 position 27250-27290. Both 34-nt (D34) and 26-nt (D26) deletion regions are illustrated in green, with the Wuhan-Hu-1 reference genome in grey. Amino acids are depicted in the colored blocks above the corresponding nucleic acids. Nucleic acid and amino acid alterations resulting from the ORF6 deletions are illustrated in a black. Image adapted from the genome visualization tool from the CoV-GLUE online resource, enabled by data from GISAID.

FIGURE 3. Replication kinetics of SARS-CoV-2 ORF6 deletion variants on BGM and Calu-3 cell lines. SARS-CoV-2 strains were inoculated on confluent BGM and Calu-3 cells at an MOI of 10^{-3} and then incubated at 36°C with 5% CO_2 for 7 days. Supernatant samples were collected at regular intervals, for which viral particle quantification was performed by qRT-PCR. Each data point is the average of three replicates, with standard deviation as error bars. Statistical analysis was performed by two-way ANOVA with Tukey multiple comparisons between both factors of comparison (virus strain and cell line) on GraphPad Prism (software version 8.4.3).

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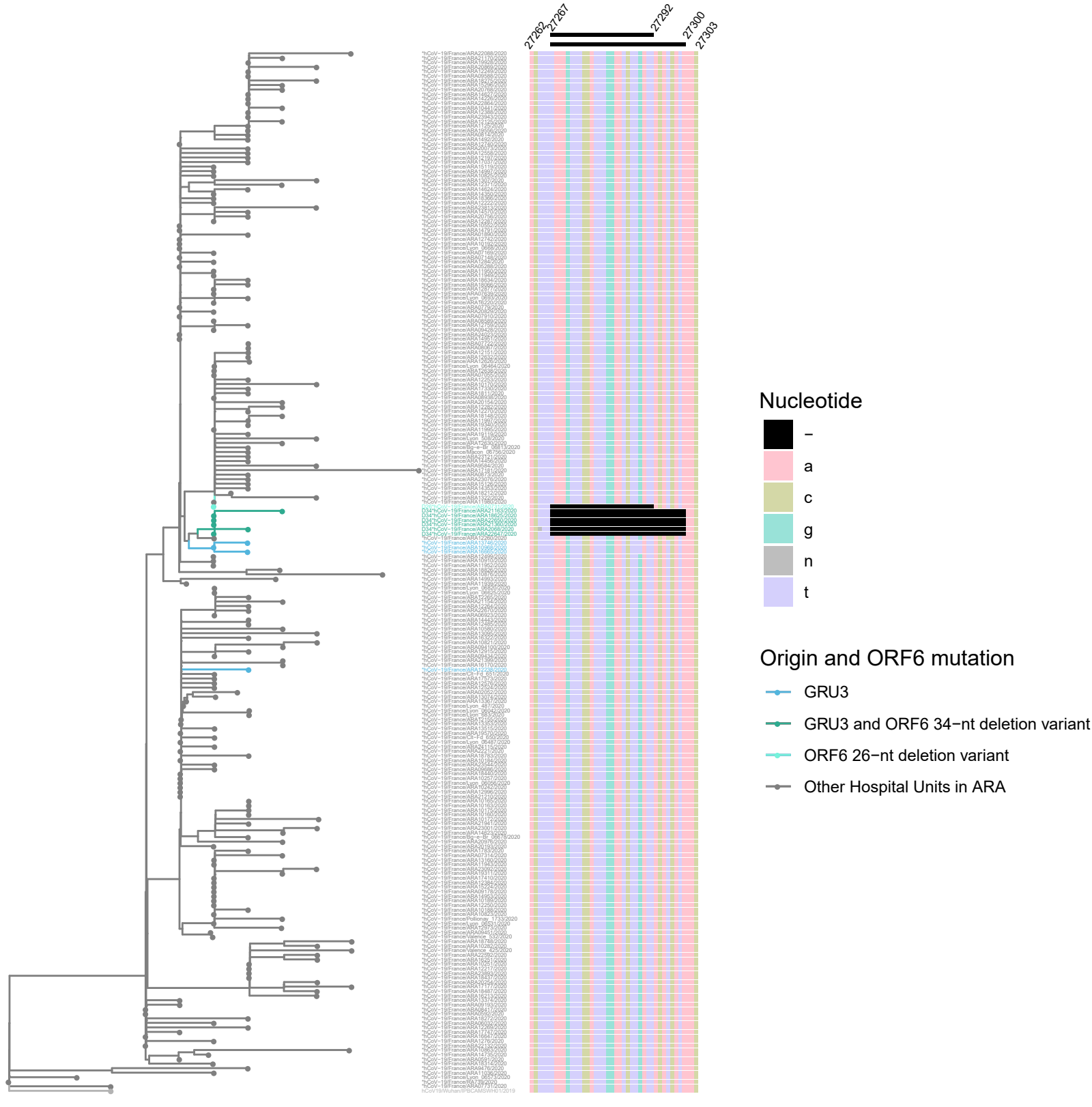
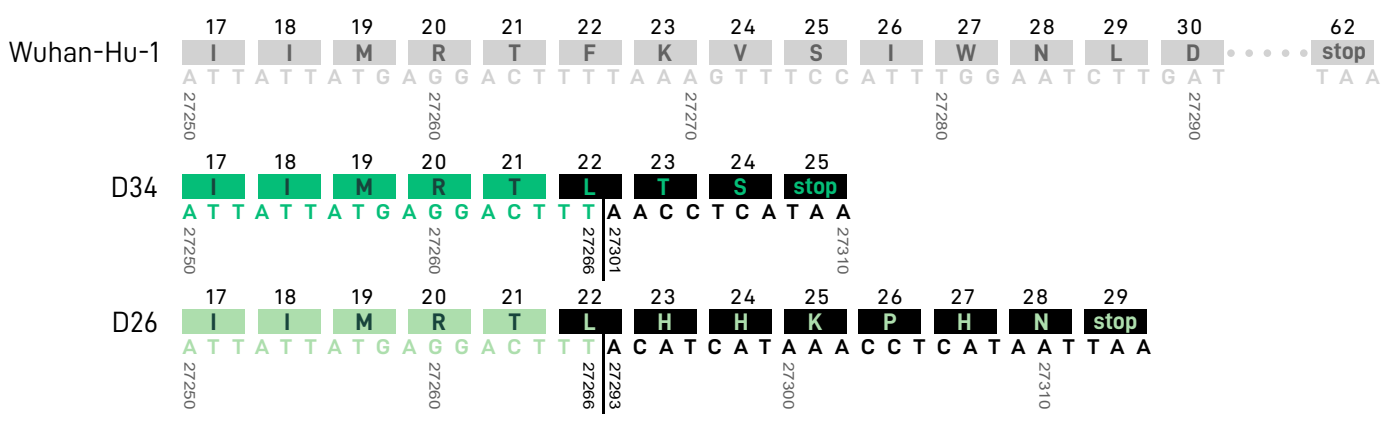

27262
27267
27292
27300
27303
Nucleotide
–
a
c
g
n
t
Origin and ORF6 mutation
GRU3
GRU3 and ORF6 34−nt deletion variant
ORF6 26−nt deletion variant
Other Hospital Units in ARA
4e−05


Wuhan-Hu-1
17 18 19 20 21 22 23 24 25 26 27 28 29 30 62
I I M R T F K V S I W N L D stop
A T T A T T A T G A G G A C T T T T A A A G T T T C C A T T T G G A A T C T T G A T T A A
27250 27260 27270 27280 27290
D34
17 18 19 20 21 22 23 24 25
I I M R T L T S stop
A T T A T T A T G A G G A C T T T A A C C T C A T A A
27250 27260 27266 27301 27310
D26
17 18 19 20 21 22 23 24 25 26 27 28 29
I I M R T L H H K P H N stop
A T T A T T A T G A G G A C T T T A C A T C A T A A A A C C T C A T A A T T A A
27250 27260 27266 27293 27300 27310

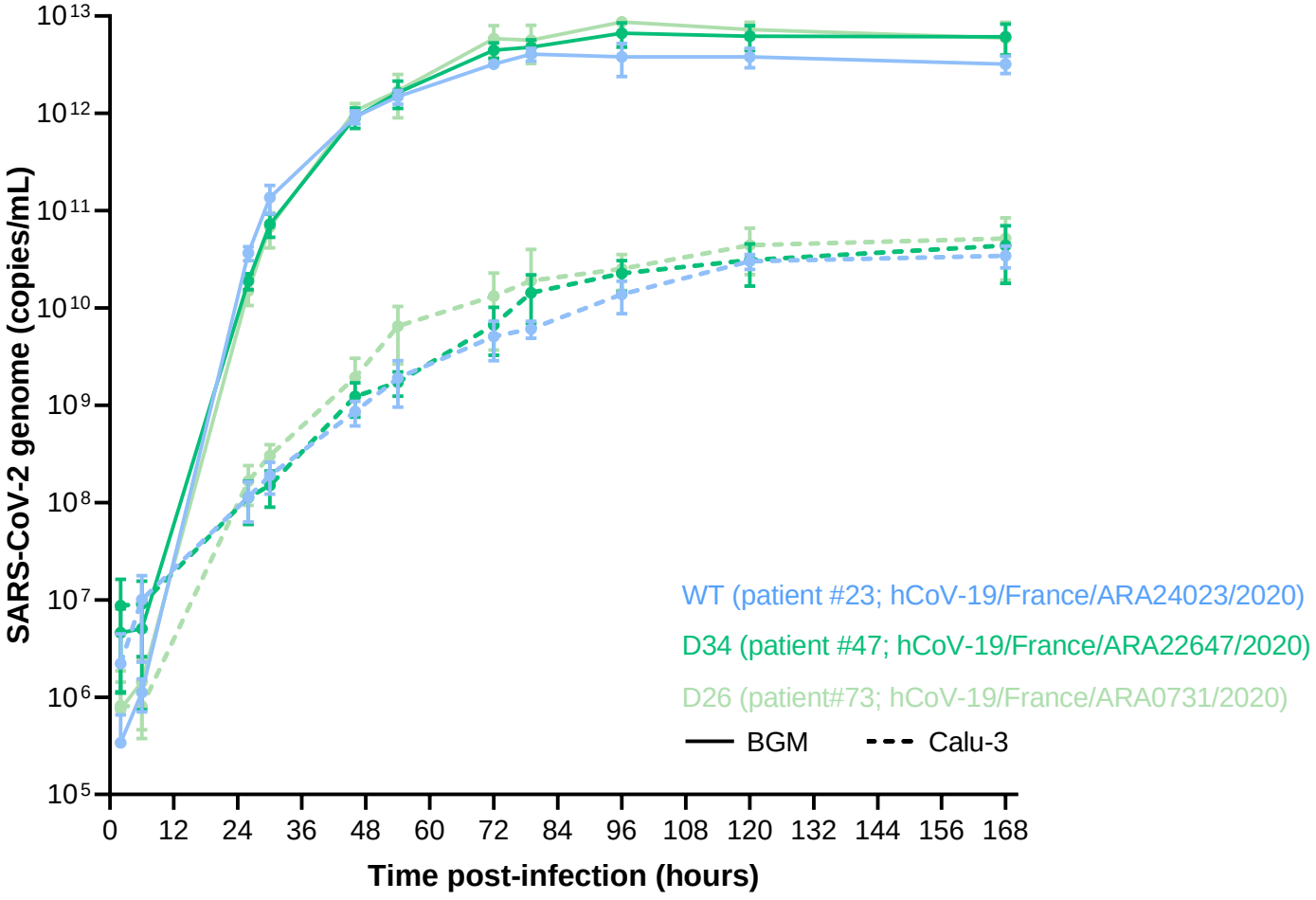

SARS-CoV-2 genome (copies/mL)
10^13
10^12
10^11
10^10
10^9
10^8
10^7
10^6
10^5
0
12
24
36
48
60
72
84
96
108
120
132
144
156
168
Time post-infection (hours)
WT (patient #23; hCoV-19/France/ARA24023/2020)
D34 (patient #47; hCoV-19/France/ARA22647/2020)
D26 (patient#73; hCoV-19/France/ARA0731/2020)
BGM
Calu-3

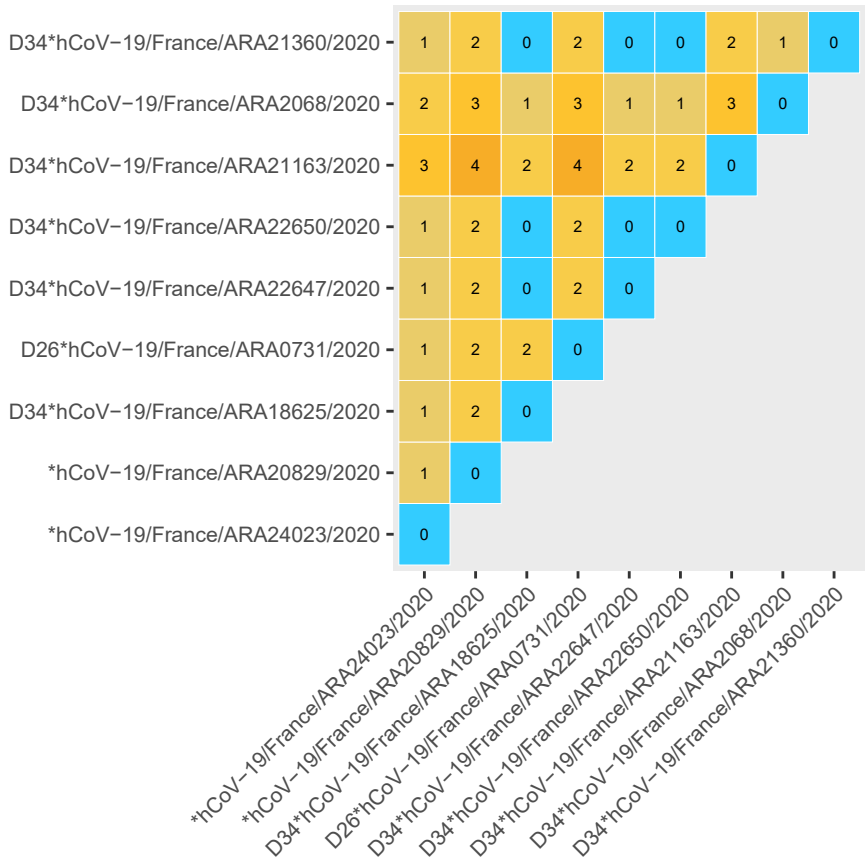
TABLE 1. Clinical data from patients infected with the ORF6 deletion variants compared with related patients infected with WT SARS-CoV-2 strains

	Patient #68	Patient #38	Patient #46	Patient #65	Patient #25	Patient #8	HCW#63	Patient #60	Patient #47	Patient #50
Sequence name[a]	ARA10968/2020	ARA12238/2020	ARA13746/2020	ARA16665/2020	ARA18625/2020	ARA2608/2020	ARA21163/2020	ARA21360/2020	ARA22647/2020	ARA22650/2020
Age (years)	89	78	84	89	97	82	31	94	81	85
Sex	F	M	F	F	M	F	F	F	M	F
Comorbidities	Hypertension	None	None	Cardiovascular disease, Hypertension	Cardiovascular disease, Hypertension	Cardiovascular disease, Hypertension, Obesity	NA	Cardiovascular disease, Hypertension	None	Cardiovascular disease
Respiratory manifestations	URTI	LRTI	LRTI	Asymptomatic	Asymptomatic	LRTI	URTI	URTI	Not specified	LRTI
Hospitalization (Yes / No)	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Hospitalization Unit	GRU-3	GRU-3	GRU-3	GRU-3	GRU-3	GRU-3	GRU-3	GRU-3	GRU-3	GRU-3
ORF6 deletion	None	None	None	None	D34	D34	D34	D34	D34	D34
Date of diagnostic	2020/03/18	2020/03/22	2020/03/25	2020/03/30	2020/04/02	2020/04/06	2020/04/07	2020/04/07	2020/04/09	2020/04/09
Duration of excretion[b]	Respiratory sample positive at D21	Not monitored	Not monitored	Respiratory sample positive at D14	Not monitored	Not monitored	Not monitored	Not monitored	Respiratory and stool samples positive at D14	Not monitored
Outcome[b]	Favorable	Favorable	Favorable	Favorable	Deceased, unrelated to COVID-19 (D5)	Deceased from COVID-19 (D6)	Favorable	Favorable	Favorable	Deceased from COVID-19 (D9)

HCW=health care worker; COPD=chronic obstructive pulmonary disease; URTI: Upper Respiratory Tract Infection; LRTI: Lower Respiratory Tract Infection; HCL=Hospices Civils de Lyon; GRU-1=geriatric rehabilitation unit within HCL; D26=26-nt deletion; D34=34-nt deletion; D=Day

[a] Sequence names in the table are preceded by hCoV-19/France/; example: hCoV-19/France/ARA0731/2020
[b] Duration of excretion and death are calculated from the date of diagnosis

SUPPLEMENTARY FIGURE 1. CoV-GLUE phylogenomic placement map. The D34 (A) and D26 (B) deletions are phylogenetically positioned against global SARS-CoV-2 sequences deposited on the GISAID database and annotated with PANGOLIN lineages. The tree was generated by the CoV-GLUE resource, which uses the RAxML (Randomized Axelerated Maximum Likelihood) software (Stamatakis 2014). Relevant deletions are in red, while WT sequences are in green.



SUPPLEMENTARY FIGURE 2. Single nucleotide polymorphism heat map of SARS-CoV-2 ORF6 WT and deletion strains. Mismatch count between consensus sequences generated by each method compared 2 by 2 for each sample. Blue tiles correspond to perfect identity and orange tiles correspond to mismatches (number of mismatches is indicated inside the tile). Matrices were generated with an R script using Decipher (alignment), ape (distance matrices) and ggplot2 (charts) libraries. Of note, undetermined bases and deletions were notconsidered in the calculation of mismatches.

SUPPLEMENTARY TABLE 1. SARS-CoV-2 genomes sequenced in the Auvergne-Rhônes-Alpes region from Feb 12 to Apr 12, 2020

Virus name	*Accession ID*	*Collection date*	*Location*	*Host*	*Gender*	*Age*	*Passage*	*Specimen*	*Lineage*	*Clade*
hCoV-19/France/RA739/2020	EPI_ISL_410486	2/8/2020	Europe / France / ARA / Contamines	Human	Female	56	Original	Oro-pharyngeal swab	B	L
hCoV-19/France/Pollionay_1733/2020	EPI_ISL_416745	3/10/2020	Europe / France / ARA / Pollionay	Human	Male	81	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Valence_425/2020	EPI_ISL_416746	3/3/2020	Europe / France / ARA / Valence	Human	Male	61	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/Lyon_487/2020	EPI_ISL_416747	3/4/2020	Europe / France / ARA / Lyon	Human	Female	43	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Lyon_508/2020	EPI_ISL_416748	3/4/2020	Europe / France / ARA / Lyon	Human	Female	50	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/Valence_532/2020	EPI_ISL_416749	3/4/2020	Europe / France / ARA / Valence	Human	Female	44	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Lyon_683/2020	EPI_ISL_416750	3/6/2020	Europe / France / ARA / Lyon	Human	Male	47	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Clermont-Ferrand_651/2020	EPI_ISL_416751	3/5/2020	Europe / France / ARA / Clermont-Ferrand	Human	Male	16	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Clermont-Ferrand_650/2020	EPI_ISL_416752	3/4/2020	Europe / France / ARA / Clermont-Ferrand	Human	Female	49	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Lyon_06464 /2020	EPI_ISL_416753	3/6/2020	Europe / France / ARA / Lyon	Human	Male	50	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/Lyon_06487/2020	EPI_ISL_416754	3/6/2020	Europe / France / ARA / Lyon	Human	Male	82	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Lyon_06531/2020	EPI_ISL_416756	3/6/2020	Europe / France / ARA / Lyon	Human	Female	88	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Bourg-en-Bresse_06678/2020	EPI_ISL_416757	3/7/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Male	41	Original		B.1	G
hCoV-19/France/Lyon_0693/2020	EPI_ISL_416758	3/8/2020	Europe / France / ARA / Lyon	Human	Male	79	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/Lyon_06042/2020	EPI_ISL_417333	3/4/2020	Europe / France / ARA / Lyon	Human	Male	48	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Lyon_06056/2020	EPI_ISL_417334	3/4/2020	Europe / France / ARA / Lyon	Human	Female	50	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Lyon_06573/2020	EPI_ISL_417335	3/6/2020	Europe / France / ARA / Lyon	Human	Male	74	Original	Nasopharyngeal swab	B	L
hCoV-19/France/Lyon_0668/2020	EPI_ISL_417336	3/6/2020	Europe / France / ARA / Lyon	Human	Male	79	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/Lyon_06625/2020	EPI_ISL_417337	3/7/2020	Europe / France / ARA / Lyon	Human	Male	78	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Macon_06756/2020	EPI_ISL_417338	3/7/2020	Europe / France / ARA / Macon	Human	Female	63	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/Lyon_06820/2020	EPI_ISL_417339	3/8/2020	Europe / France / ARA / Lyon	Human	Female	86	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/Bourg-en-Bresse_06813/2020	EPI_ISL_417340	3/7/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Male	53	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA094100/2020	EPI_ISL_418412	3/15/2020	Europe / France / ARA / Privas	Human	Female	55	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA09428/2020	EPI_ISL_418413	3/15/2020	Europe / France / ARA / Macon	Human	Female	80	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA09434/2020	EPI_ISL_418414	3/15/2020	Europe / France / ARA / Valence	Human	Female	84	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA09451/2020	EPI_ISL_418415	3/15/2020	Europe / France / ARA / Valence	Human	Female	93	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA09588/2020	EPI_ISL_418416	3/16/2020	Europe / France / ARA / Venissieux	Human	Female	41	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA09686/2020	EPI_ISL_418417	3/16/2020	Europe / France / ARA / Valence	Human	Male	61	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10163/2020	EPI_ISL_418418	3/16/2020	Europe / France / ARA / Lyon	Human	Female	58	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10165/2020	EPI_ISL_418419	3/16/2020	Europe / France / ARA / Lyon	Human	Male	30	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10170/2020	EPI_ISL_418420	3/17/2020	Europe / France / ARA / Lyon	Human	Female	40	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA10172/2020	EPI_ISL_418421	3/17/2020	Europe / France / ARA / Lyon	Human	Female	43	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10184/2020	EPI_ISL_418422	3/17/2020	Europe / France / ARA / Lyon	Human	Female	76	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10188/2020	EPI_ISL_418423	3/17/2020	Europe / France / ARA / Lyon	Human	Female	73	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10189/2020	EPI_ISL_418424	3/17/2020	Europe / France / ARA / Lyon	Human	Female	79	Original	Nasopharyngeal swab	B.1	G

hCoV-19/France/ARA10192/2020	EPI_ISL_418425	3/17/2020	Europe / France / ARA / Lyon	Human	Female	82	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA10251/2020	EPI_ISL_418426	3/17/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Male	61	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA10257/2020	EPI_ISL_418427	3/17/2020	Europe / France / ARA / Saint-Priest	Human	Female	56	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10282/2020	EPI_ISL_418428	3/17/2020	Europe / France / ARA / Vienne	Human	Male	NA	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA10876/2020	EPI_ISL_418429	3/18/2020	Europe / France / ARA / Lyon	Human	Female	61	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA10910/2020	EPI_ISL_418430	3/18/2020	Europe / France / ARA / Lyon	Human	Female	85	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA10968/2020	EPI_ISL_418431	3/18/2020	Europe / France / ARA / Lyon	Human	Female	90	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA11036/2020	EPI_ISL_418432	3/18/2020	Europe / France / ARA / Lyon	Human	Male	60	Original	Nasopharyngeal swab	B.2	V
hCoV-19/France/ARA10552/2020	EPI_ISL_419168	3/17/2020	Europe / France / ARA / Valence	Human	Male	0	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA11939/2020	EPI_ISL_419169	3/21/2020	Europe / France / ARA / Lyon	Human	Female	42	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA11943/2020	EPI_ISL_419170	3/21/2020	Europe / France / ARA / Lyon	Human	Female	31	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA11949/2020	EPI_ISL_419171	3/21/2020	Europe / France / ARA / Lyon	Human	Male	60	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA11950/2020	EPI_ISL_419172	3/21/2020	Europe / France / ARA / Lyon	Human	Male	67	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA11952/2020	EPI_ISL_419173	3/21/2020	Europe / France / ARA / Lyon	Human	Female	44	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA11980/2020	EPI_ISL_419174	3/20/2020	Europe / France / ARA / Macon	Human	Male	83	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA11995/2020	EPI_ISL_419175	3/21/2020	Europe / France / ARA / Macon	Human	Male	85	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA11997/2020	EPI_ISL_419176	3/21/2020	Europe / France / ARA / Macon	Human	Male	43	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12125/2020	EPI_ISL_419177	3/22/2020	Europe / France / ARA / Lyon	Human	Female	56	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12217/2020	EPI_ISL_419178	3/22/2020	Europe / France / ARA / Lyon	Human	Female	52	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA12222/2020	EPI_ISL_419179	3/22/2020	Europe / France / ARA / Lyon	Human	Male	88	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12238/2020	EPI_ISL_419180	3/22/2020	Europe / France / ARA / Lyon	Human	Male	78	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12249/2020	EPI_ISL_419181	3/22/2020	Europe / France / ARA / Lyon	Human	Female	40	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12250/2020	EPI_ISL_419182	3/22/2020	Europe / France / ARA / Lyon	Human	Female	54	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12253/2020	EPI_ISL_419183	3/22/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Male	86	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12260/2020	EPI_ISL_419184	3/22/2020	Europe / France / ARA / Lyon	Human	Male	73	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12264/2020	EPI_ISL_419185	3/22/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Female	88	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12265/2020	EPI_ISL_419186	3/22/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Female	96	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12269/2020	EPI_ISL_419187	3/22/2020	Europe / France / ARA / Macon	Human	Male	60	Original	Nasopharyngeal aspirate	B.1	G
hCoV-19/France/ARA12270/2020	EPI_ISL_419188	3/22/2020	Europe / France / ARA / Macon	Human	Female	53	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12371/2020	EPI_ISL_420604	3/23/2020	Europe / France / ARA / Lyon	Human	Male	93	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12384/2020	EPI_ISL_420605	3/22/2020	Europe / France / ARA / Lyon	Human	Male	88	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12388/2020	EPI_ISL_420606	3/22/2020	Europe / France / ARA / Lyon	Human	Male	81	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12485/2020	EPI_ISL_420607	3/23/2020	Europe / France / ARA / Lyon	Human	Male	88	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12499/2020	EPI_ISL_420608	3/23/2020	Europe / France / ARA / Lyon	Human	Female	85	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12524/2020	EPI_ISL_420609	3/23/2020	Europe / France / ARA / Lyon	Human	Female	85	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12558/2020	EPI_ISL_420610	3/23/2020	Europe / France / ARA / Lyon	Human	Female	85	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12576/2020	EPI_ISL_420611	3/23/2020	Europe / France / ARA / Lyon	Human	Male	26	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12626/2020	EPI_ISL_420612	3/23/2020	Europe / France / ARA / Macon	Human	Female	58	Original	Nasopharyngeal aspirate	B.1	GH

hCoV-19/France/ARA12630/2020	EPI_ISL_420613	3/23/2020	Europe / France / ARA / Macon	Human	Female	47	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12632/2020	EPI_ISL_420614	3/23/2020	Europe / France / ARA / Macon	Human	Female	38	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12759/2020	EPI_ISL_420615	3/23/2020	Europe / France / ARA / Lyon	Human	Male	84	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA1284/2020	EPI_ISL_420616	3/23/2020	Europe / France / ARA / Lyon	Human	Female	87	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12877/2020	EPI_ISL_420617	3/23/2020	Europe / France / ARA / Lyon	Human	Male	28	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA12915/2020	EPI_ISL_420618	3/23/2020	Europe / France / ARA / Lyon	Human	Male	71	Original	Nasopharyngeal aspirate	B.1	G
hCoV-19/France/ARA12973/2020	EPI_ISL_420619	3/23/2020	Europe / France / ARA / Lyon	Human	Female	87	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12996/2020	EPI_ISL_420620	3/23/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Female	86	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA1307/2020	EPI_ISL_420621	3/24/2020	Europe / France / ARA / Lyon	Human	Female	23	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA13074/2020	EPI_ISL_420622	3/24/2020	Europe / France / ARA / Lyon	Human	Male	59	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA13095/2020	EPI_ISL_420623	3/24/2020	Europe / France / ARA / Lyon	Human	Male	66	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA13160/2020	EPI_ISL_420624	3/24/2020	Europe / France / ARA / Lyon	Human	Female	50	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA1322/2020	EPI_ISL_420625	3/24/2020	Europe / France / ARA / Lyon	Human	Male	47	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA01890/2020	EPI_ISL_508871	3/18/2020	Europe / France / ARA / Craponne	Human	Female	50	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA07639/2020	EPI_ISL_508872	3/11/2020	Europe / France / ARA / Lyon	Human	Female	91	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA07910/2020	EPI_ISL_508873	3/12/2020	Europe / France / ARA / Lyon	Human	Female	85	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA08589/2020	EPI_ISL_508874	3/13/2020	Europe / France / ARA / Lyon	Human	Female	57	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA0873/2020	EPI_ISL_508875	3/14/2020	Europe / France / ARA / Macon	Human	Female	39	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA08938/2020	EPI_ISL_508876	3/14/2020	Europe / France / ARA / Macon	Human	Male	58	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA09178/2020	EPI_ISL_508877	3/15/2020	Europe / France / ARA / Lyon	Human	Female	49	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA09193/2020	EPI_ISL_508878	3/15/2020	Europe / France / ARA / Venissieux	Human	Male	64	Original	Nasopharyngeal swab	B.1.11	G
hCoV-19/France/ARA10160/2020	EPI_ISL_508879	3/16/2020	Europe / France / ARA / Lyon	Human	Male	43	Original	Nasopharyngeal aspirate	B.1	G
hCoV-19/France/ARA10175/2020	EPI_ISL_508880	3/16/2020	Europe / France / ARA / Lyon	Human	Male	58	Original	Nasopharyngeal aspirate	B.1	G
hCoV-19/France/ARA10242/2020	EPI_ISL_508881	3/16/2020	Europe / France / ARA / Valence	Human	Female	82	Original	Nasopharyngeal aspirate	B.1	G
hCoV-19/France/ARA10823/2020	EPI_ISL_508882	3/18/2020	Europe / France / ARA / Lyon	Human	Female	60	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10825/2020	EPI_ISL_508883	3/18/2020	Europe / France / ARA / Lyon	Human	Female	29	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14226/2020	EPI_ISL_508884	3/25/2020	Europe / France / ARA / Lyon	Human	Male	88	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14350/2020	EPI_ISL_508885	3/26/2020	Europe / France / ARA / Lyon	Human	Female	44	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14353/2020	EPI_ISL_508886	3/24/2020	Europe / France / ARA / Lyon	Human	Male	32	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14443/2020	EPI_ISL_508887	3/26/2020	Europe / France / ARA / Lyon	Human	Female	46	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA14456/2020	EPI_ISL_508888	3/26/2020	Europe / France / ARA / Lyon	Human	Male	26	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14570/2020	EPI_ISL_508889	3/26/2020	Europe / France / ARA / Lyon	Human	Male	50	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14623/2020	EPI_ISL_508890	3/26/2020	Europe / France / ARA / Lyon	Human	Male	72	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA14624/2020	EPI_ISL_508891	3/26/2020	Europe / France / ARA / Lyon	Human	Female	81	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14627/2020	EPI_ISL_508892	3/26/2020	Europe / France / ARA / Lyon	Human	Female	52	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14735/2020	EPI_ISL_508893	3/26/2020	Europe / France / ARA / Lyon	Human	Male	91	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA14791/2020	EPI_ISL_508894	3/26/2020	Europe / France / ARA / Lyon	Human	Male	73	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA1492/2020	EPI_ISL_508895	3/26/2020	Europe / France / ARA / Lyon	Human	Female	47	Original	Nasopharyngeal swab	B.1	GH

hCoV-19/France/ARA14951/2020	EPI_ISL_508896	3/27/2020	Europe / France / ARA / Lyon	Human	Female	32	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA14953/2020	EPI_ISL_508897	3/27/2020	Europe / France / ARA / Lyon	Human	Female	51	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA14993/2020	EPI_ISL_508898	3/27/2020	Europe / France / ARA / Lyon	Human	Female	93	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA14997/2020	EPI_ISL_508899	3/27/2020	Europe / France / ARA / Lyon	Human	Female	89	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA15119/2020	EPI_ISL_508900	3/27/2020	Europe / France / ARA / Lyon	Human	Male	39	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA15126/2020	EPI_ISL_508901	3/27/2020	Europe / France / ARA / Lyon	Human	Male	22	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA15224/2020	EPI_ISL_508902	3/27/2020	Europe / France / ARA / Lyon	Human	Female	41	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA15296/2020	EPI_ISL_508903	3/27/2020	Europe / France / ARA / Lyon	Human	Female	69	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA16170/2020	EPI_ISL_508904	3/29/2020	Europe / France / ARA / Lyon	Human	Male	72	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA16213/2020	EPI_ISL_508905	3/29/2020	Europe / France / ARA / Lyon	Human	Female	83	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA16220/2020	EPI_ISL_508906	3/29/2020	Europe / France / ARA / Lyon	Human	Male	80	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA16251/2020	EPI_ISL_508907	3/29/2020	Europe / France / ARA / Lyon	Human	Male	86	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA16322/2020	EPI_ISL_508908	3/30/2020	Europe / France / ARA / Lyon	Human	Male	83	Original	Nasopharyngeal aspirate	B.1	G
hCoV-19/France/ARA20756/2020	EPI_ISL_508912	4/6/2020	Europe / France / ARA / Lyon	Human	Female	27	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA20768/2020	EPI_ISL_508913	4/6/2020	Europe / France / ARA / Lyon	Human	Female	97	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA20829/2020	EPI_ISL_508914	4/6/2020	Europe / France / ARA / Lyon	Human	Female	36	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA20976/2020	EPI_ISL_508915	4/6/2020	Europe / France / ARA / Lyon	Human	Male	81	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA21170/2020	EPI_ISL_508916	4/7/2020	Europe / France / ARA / Lyon	Human	Female	42	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA2221/2020	EPI_ISL_508917	4/8/2020	Europe / France / ARA / Lyon	Human	Female	91	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA22592/2020	EPI_ISL_508918	4/9/2020	Europe / France / ARA / Lyon	Human	Male	26	Original	Nasopharyngeal swab	B.1.1.7	GR
hCoV-19/France/ARA22647/2020	EPI_ISL_508919	4/9/2020	Europe / France / ARA / Lyon	Human	Male	80	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA22650/2020	EPI_ISL_508920	4/9/2020	Europe / France / ARA / Lyon	Human	Female	84	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA22670/2020	EPI_ISL_508921	4/9/2020	Europe / France / ARA / Lyon	Human	Male	88	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA22864/2020	EPI_ISL_508922	4/9/2020	Europe / France / ARA / Lyon	Human	Female	98	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA23001/2020	EPI_ISL_508923	4/10/2020	Europe / France / ARA / Lyon	Human	Male	49	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA23076/2020	EPI_ISL_508924	4/10/2020	Europe / France / ARA / Lyon	Human	Male	55	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA23092/2020	EPI_ISL_508925	4/10/2020	Europe / France / ARA / Lyon	Human	Female	61	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA23121/2020	EPI_ISL_508926	4/10/2020	Europe / France / ARA / Lyon	Human	Female	82	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA23544/2020	EPI_ISL_508927	4/11/2020	Europe / France / ARA / Lyon	Human	Male	60	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA23813/2020	EPI_ISL_508928	4/11/2020	Europe / France / ARA / Lyon	Human	Male	23	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA23893/2020	EPI_ISL_508929	4/11/2020	Europe / France / ARA / Lyon	Human	Male	89	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA23943/2020	EPI_ISL_508930	4/12/2020	Europe / France / ARA / Lyon	Human	Female	63	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA24023/2020	EPI_ISL_508931	4/11/2020	Europe / France / ARA / Tarare	Human	Female	25	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA24115/2020	EPI_ISL_508932	4/12/2020	Europe / France / ARA / Villefranche	Human	Female	45	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA05288/2020	EPI_ISL_508933	2/28/2020	Europe / France / ARA / Lyon	Human	Female	78	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA0591/2020	EPI_ISL_508934	3/1/2020	Europe / France / ARA / Chambery	Human	Male	29	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA0592/2020	EPI_ISL_508935	3/2/2020	Europe / France / ARA / Chambery	Human	Female	48	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA06032/2020	EPI_ISL_508936	3/4/2020	Europe / France / ARA / Chambery	Human	Male	57	Original	Nasopharyngeal swab	B.1	G

hCoV-19/France/ARA06923/2020	EPI_ISL_508937 3/9/2020	Europe / France / ARA / Lyon	Human	Female	78	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA07055/2020	EPI_ISL_508938 3/9/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Female	73	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA07148/2020	EPI_ISL_508939 3/9/2020	Europe / France / ARA / Lyon	Human	Female	90	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA07169/2020	EPI_ISL_508940 3/9/2020	Europe / France / ARA / Lyon	Human	Female	32	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA0731/2020	EPI_ISL_508941 3/10/2020	Europe / France / ARA / Macon	Human	Male	93	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA07314/2020	EPI_ISL_508942 3/10/2020	Europe / France / ARA / Lyon	Human	Female	90	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA07722/2020	EPI_ISL_508943 3/11/2020	Europe / France / ARA / Macon	Human	Male	72	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA07731/2020	EPI_ISL_508944 3/11/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Male	33	Original	Nasopharyngeal swab	B	L
hCoV-19/France/ARA0779/2020	EPI_ISL_508945 3/11/2020	Europe / France / ARA / Macon	Human	Female	72	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA08067/2020	EPI_ISL_508946 3/12/2020	Europe / France / ARA / Macon	Human	Male	63	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA0814/2020	EPI_ISL_508947 3/12/2020	Europe / France / ARA / Vienne	Human	Female	61	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA08417/2020	EPI_ISL_508948 3/13/2020	Europe / France / ARA / Lyon	Human	Male	92	Original	Nasopharyngeal aspirate	B.1	G
hCoV-19/France/ARA12155/2020	EPI_ISL_508949 3/21/2020	Europe / France / ARA / Macon	Human	Female	57	Original	Nasopharyngeal aspirate	B.1	G
hCoV-19/France/ARA12282/2020	EPI_ISL_508950 3/22/2020	Europe / France / ARA / Macon	Human	Male	34	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12287/2020	EPI_ISL_508951 3/22/2020	Europe / France / ARA / Lyon	Human	Female	90	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12638/2020	EPI_ISL_508952 3/23/2020	Europe / France / ARA / Macon	Human	Male	49	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12742/2020	EPI_ISL_508953 3/23/2020	Europe / France / ARA / Lyon	Human	Male	92	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA13353/2020	EPI_ISL_508954 3/24/2020	Europe / France / ARA / Lyon	Human	Female	34	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA13367/2020	EPI_ISL_508955 3/24/2020	Europe / France / ARA / Lyon	Human	Female	82	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA13374/2020	EPI_ISL_508956 3/24/2020	Europe / France / ARA / Lyon	Human	Male	93	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA13515/2020	EPI_ISL_508957 3/24/2020	Europe / France / ARA / Lyon	Human	Male	86	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA17177/2020	EPI_ISL_508958 3/30/2020	Europe / France / ARA / Contamine-sur-Arve	Human	Female	55	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA17330/2020	EPI_ISL_508959 3/31/2020	Europe / France / ARA / Lyon	Human	Male	96	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA17747/2020	EPI_ISL_508960 3/31/2020	Europe / France / ARA / Lyon	Human	Male	78	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA1783/2020	EPI_ISL_508961 4/1/2020	Europe / France / ARA / Lyon	Human	Male	90	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA1811/2020	EPI_ISL_508962 4/1/2020	Europe / France / ARA / Lyon	Human	Male	83	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA18212/2020	EPI_ISL_508963 4/1/2020	Europe / France / ARA / Lyon	Human	Male	88	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA18272/2020	EPI_ISL_508964 4/2/2020	Europe / France / ARA / Lyon	Human	Male	56	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA18275/2020	EPI_ISL_508965 4/2/2020	Europe / France / ARA / Lyon	Human	Male	69	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA18314/2020	EPI_ISL_508966 4/2/2020	Europe / France / ARA / Bourgoin-Jallieu	Human	Female	43	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA18366/2020	EPI_ISL_508967 4/2/2020	Europe / France / ARA / Lyon	Human	Female	85	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA18437/2020	EPI_ISL_508968 4/2/2020	Europe / France / ARA / Bourg-en-Bresse	Human	Female	30	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA18440/2020	EPI_ISL_508969 4/2/2020	Europe / France / ARA / Lyon	Human	Female	27	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA18487/2020	EPI_ISL_508970 4/2/2020	Europe / France / ARA / Lyon	Human	Female	50	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA18625/2020	EPI_ISL_508971 4/2/2020	Europe / France / ARA / Lyon	Human	Male	96	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA18634/2020	EPI_ISL_508972 4/2/2020	Europe / France / ARA / Lyon	Human	Male	52	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA18748/2020	EPI_ISL_508973 4/2/2020	Europe / France / ARA / Lyon	Human	Female	88	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA18783/2020	EPI_ISL_508974 4/3/2020	Europe / France / ARA / Lyon	Human	Female	38	Original	Nasopharyngeal swab	B.1	G

hCoV-19/France/ARA18826/2020	EPI_ISL_508975 4/2/2020	Europe / France / ARA / Bourgoin-Jallieu	Human	Female	70	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA19119/2020	EPI_ISL_508976 4/1/2020	Europe / France / ARA / Decines	Human	Female	29	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA19311/2020	EPI_ISL_508977 4/3/2020	Europe / France / ARA / Lyon	Human	Female	22	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA19340/2020	EPI_ISL_508978 4/3/2020	Europe / France / ARA / Villefranche	Human	Female	37	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA19556/2020	EPI_ISL_508979 4/3/2020	Europe / France / ARA / Lyon	Human	Male	33	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA19570/2020	EPI_ISL_508980 4/3/2020	Europe / France / ARA / Lyon	Human	Male	65	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA19928/2020	EPI_ISL_508981 4/4/2020	Europe / France / ARA / Lyon	Human	Male	77	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA20073/2020	EPI_ISL_508982 4/5/2020	Europe / France / ARA / Lyon	Human	Male	92	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA20154/2020	EPI_ISL_508983 4/5/2020	Europe / France / ARA / Lyon	Human	Female	79	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA20193/2020	EPI_ISL_508984 4/5/2020	Europe / France / ARA / Lyon	Human	Female	34	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA20254/2020	EPI_ISL_508985 4/5/2020	Europe / France / ARA / Lyon	Human	Male	81	Original	Nasopharyngeal swab	B.1.1	GR
hCoV-19/France/ARA13746/2020	EPI_ISL_508986 3/25/2020	Europe / France / ARA / Lyon	Human	Female	84	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA16665/2020	EPI_ISL_508987 3/30/2020	Europe / France / ARA / Lyon	Human	Female	89	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA2068/2020	EPI_ISL_508988 4/6/2020	Europe / France / ARA / Lyon	Human	Female	82	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA21360/2020	EPI_ISL_508989 4/7/2020	Europe / France / ARA / Lyon	Human	Female	94	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA20869/2020	EPI_ISL_508990 4/6/2020	Europe / France / ARA / Lyon	Human	Female	56	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA21154/2020	EPI_ISL_508991 4/7/2020	Europe / France / ARA / Lyon	Human	Female	57	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA21163/2020	EPI_ISL_508992 4/7/2020	Europe / France / ARA / Lyon	Human	Female	30	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA21210/2020	EPI_ISL_508993 4/7/2020	Europe / France / ARA / Lyon	Human	Male	41	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA21399/2020	EPI_ISL_508994 4/7/2020	Europe / France / ARA / Lyon	Human	Female	32	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA21941/2020	EPI_ISL_508995 4/8/2020	Europe / France / ARA / Lyon	Human	Male	48	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA22088/2020	EPI_ISL_508996 4/8/2020	Europe / France / ARA / Lyon	Human	Female	91	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA22132/2020	EPI_ISL_508997 4/8/2020	Europe / France / ARA / Lyon	Human	Male	29	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10441/2020	EPI_ISL_508998 3/17/2020	Europe / France / ARA / Bourgoin-Jallieu	Human	Female	71	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA10580/2020	EPI_ISL_508999 3/18/2020	Europe / France / ARA / Lyon	Human	Male	72	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10821/2020	EPI_ISL_509000 3/18/2020	Europe / France / ARA / Lyon	Human	Male	30	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA10863/2020	EPI_ISL_509001 3/18/2020	Europe / France / ARA / Lyon	Human	Female	86	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA1125/2020	EPI_ISL_509002 3/19/2020	Europe / France / ARA / Lyon	Human	Female	26	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA9584/2020	EPI_ISL_509003 3/16/2020	Europe / France / ARA / Venissieux	Human	Male	58	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA9476/2020	EPI_ISL_509004 3/16/2020	Europe / France / ARA / Venissieux	Human	Male	51	Original	Nasopharyngeal swab	B.2.1	V
hCoV-19/France/ARA12151/2020	EPI_ISL_509005 3/21/2020	Europe / France / ARA / Macon	Human	Male	84	Original	Nasopharyngeal aspirate	B.1	GH
hCoV-19/France/ARA12197/2020	EPI_ISL_509006 3/22/2020	Europe / France / ARA / Villefranche	Human	Female	NA	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA1276/2020	EPI_ISL_509007 3/23/2020	Europe / France / ARA / Lyon	Human	Female	48	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA12740/2020	EPI_ISL_509008 3/23/2020	Europe / France / ARA / Lyon	Human	Female	67	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA16647/2020	EPI_ISL_509009 3/25/2020	Europe / France / ARA / Lyon	Human	Male	83	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA02052/2020	EPI_ISL_509010 3/30/2020	Europe / France / ARA / Lyon	Human	Female	79	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA17037/2020	EPI_ISL_509011 3/31/2020	Europe / France / ARA / Lyon	Human	Male	49	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA17181/2020	EPI_ISL_509012 3/30/2020	Europe / France / ARA / Contamine-sur-Arve	Human	Female	26	Original	Nasopharyngeal swab	B.1	GH

hCoV-19/France/ARA17410/2020	EPI_ISL_509013 3/31/2020	Europe / France / ARA / Lyon	Human	Female	55	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA17573/2020	EPI_ISL_509014 3/31/2020	Europe / France / ARA / Lyon	Human	Female	75	Original	Nasopharyngeal swab	B.1	G
hCoV-19/France/ARA18066/2020	EPI_ISL_509015 4/1/2020	Europe / France / ARA / Villefranche	Human	Male	72	Original	Nasopharyngeal swab	B.1	GH
hCoV-19/France/ARA18148/2020	EPI_ISL_509016 4/1/2020	Europe / France / ARA / Oyonnax	Human	Male	58	Original	Nasopharyngeal swab	B.1	GH