Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Preliminary data on severe SARS-CoV-2 infection caused by the 501Y.V2 variant

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To the Editor,

In January 2021, the incidence of COVID-19 and its mortality started rising for the third time in France. This rise may associate with three emerging variants, namely, V1, V2, and V3, which are the 20I/501Y.V1 (“English”), 20H/501Y.V2 (“South African”), and 20J/501Y.V3 (“Brazilian”) variants, respectively. V1 was recently suggested to increase mortality in people in the UK who tested positive for COVID-19 on community screening [1]. It is now responsible for most (66%) new cases in France whereas V2 and V3 together currently account for 5% of all positive polymerase-chain reaction tests [2].

In early 2021, V2/V3 spread to the Moselle department located in the Grand-Est (northeast) region. By February, V2/V3 prevalence was 41% [3]. However, the most recent epidemiological Flash surveys with precise sequencing show that only V2 is circulating in Moselle [4].

Very little is known about V2 infection, including its outcomes relative to other strains.

Here, we aimed to report the preliminary observational data of consecutive COVID-19 critically ill patients infected by V2, who were hospitalised in a 52-bed intensive care unit (ICU) in Moselle, between the 3rd of February and the 16th of March 2021.

We conducted a retrospective monocentric study including all consecutive adult patients with laboratory confirmed SARS-CoV-2 infection with variant screening admitted to the ICU for acute respiratory failure between the 3rd of February and the 16th of March 2021. Clinical electronic medical records, nursing records, laboratory and radiological findings were reviewed, and demographics, comorbidities, supportive therapy needs and vital status at 60 days after ICU admission for all patients were collected.

We compared patients with V2, V1, and wild-type virus in terms of demographic, ICU scores, comorbidities, biological data, chest computed tomodensitometry and outcomes.

Continuous and categorical variables were described as median (interquartile range [IQR]) and as frequency (percentages). Comparisons used Kruskal–Wallis and Fisher’s exact tests when appropriate. Independent risk factors of Day 60 mortality in patients with V1 or V2 infection were explored through a multivariate logistic regression. The significance level was set at 5%. The association measures were calculated (adjusted odds ratio) with a confidence interval of 95%. Kaplan–Meier estimator was used to express the survival probability from time to inclusion to Day 60 and log-rank test was performed. All analyses were performed by using SAS 9.4 (SAS Inst., Cary, NC).

The study was carried out in accordance with the French law was registered with ClinicalTrials.gov under identification number NCT 04430322. Patients (or their relatives if any) were notified about the anonym use of their healthcare data via an information letter. Need for informed consent was waived as regard to the study observational design.

One hundred and thirty-one consecutive patients with severe SARS-CoV-2 infection confirmed by polymerase chain reaction were admitted to ICU during the study period. None were hospitalised for reinfection. All patients received early corticosteroids and intermediate or full-dose thromboprophylaxis at ICU admission.

Variant screening of 104 (80%) patient respiratory samples showed that 60 (58%), 33 (32%), and 11 (10%) patients had V2, V1, and the wild-type strain, respectively. Median age of V2-infected patients was 63 (56-69) and 36 (60%) were of male gender. The V2–infected cohort also included three between pregnant women aged 32–40 years old. Obesity, hypertension, diabetes were the main comorbidities (Table 1). Thirty-four patients (57%) required mechanical ventilation and 4 patients were treated by veno-venous extracorporeal membrane oxygenation. By the 16th of May 2021, all V2-infected patients were discharged from the ICU. Eighteen (30%) patients died in the ICU and 4 (7%) patients were still hospitalised. Table 1 compares the patients with V2, V1, and wild-type virus in terms of demographic, ICU scores, comorbidities, biological data, chest computed tomodensitometry and outcomes. Even if there were differences in age, sex ratio, D-dimers, fibrinogen, mechanical ventilation requirement and mortality rate in V2-infected patients, none of them between the three groups were significant after Bonferroni correction.

The relation between B.1.1.7 (V1) or 501Y.V2 (V2) SARS-CoV-2 strain and 60-day mortality was explored through a multivariate logistic regression (Table 2). V2 was highly associated with 60-day mortality (odds ratio, 5.67; 95% Confidence Interval, 1.04–30.81).

The Kaplan–Meier survival analysis showed significant difference between the two variants of concern (VOC) (p = 0,03) (Fig. 1).

Abbreviations: AKI, Acute Kidney Injury; CT, computed tomodensitometry; FiO2, fraction of inspired oxygen; ICU, Intensive Care Unit; MV, mechanical ventilation; PaO2, partial pressure of oxygen; SAPS, simplified acute physiology score; SOFA, Sequential Organ Failure Assessment; VOC, variant of concern.*Keywords:* COVID-19; Variants; Acute respiratory failure.

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Table 1
Demographic, clinical, and resuscitation care characteristics of the 104 patients who were admitted to the ICU between the 3rd of February and the 16th of March 2021. Patients were divided according to the SARS-CoV-2 strain in their respiratory sample.

	All patients (n = 104)	Wild-type strain (n = 11)	B.1.1.7 (V1) (n = 33)	501Y.V2 (V2) (n = 60)	*P* value
Patients' characteristics					
Age, years	63 (53–69)	67 (59–69)	58 (49–65)	63 (56–69)	0.15
Women	38 (37)	6 (55)	8 (24)	24 (40)	0,07
Pregnant women	4 (4)	0 (0)	1 (3)	3 (5)	0.99
Body mass index, kg/m^2	31 (27–35)	31 (26 (32)	32 (27–37)	30 (27–34)	0.65
$<$ 25 kg/m^2	18 (17)	2 (18)	7 (21)	9 (15)	0.72
25−30 kg/m^2	27 (26)	2 (18)	7 (21)	18 (30)	
30−35 kg/m^2	35 (34)	5 (45)	8 (24)	22 (37)	
35−40 kg/m^2	12 (12)	1 (9)	6 (18)	5 (9)	
$\geq$ 40 kg/m^2	12 (12)	1 (9)	5 (15)	6 (10)	
ICU scores					
SAPS II score	40 (28–56)	53 (31–58)	35 (30–51)	41 (26–55)	0.60
SOFA score at ICU admission	5 (4–7)	5 (4–7)	5 (4–6)	5 (4–7)	0.92
Main comorbidities					
Arterial hypertension	48 (46)	6 (55)	11 (33)	31 (52)	0.22
Diabetes mellitus	34 (33)	5 (45)	10 (30)	19 (32)	0.65
Immunodeficiency[a]	4 (4)	0 (0)	2 (6)	2 (3)	0.75
Cardiovascular disease	17 (16)	2 (18)	3 (9)	12 (20)	0.42
Chronic renal failure	6 (6)	1 (9)	3 (9)	2 (3)	0.34
Chest CT					
Parenchymal involvement (%)					
$<$ 10	2 (2)	0 (0)	0 (0)	2 (4)	0.89
10−25	8 (8)	0 (0)	3 (9)	5 (9)	
25−50	34 (34)	4 (40)	13 (40)	17 (30)	
50−75	39 (39)	5 (50)	13 (40)	21 (37)	
$\geq$ 75	17 (17)	1 (10)	4 (12)	12 (21)	
Pulmonary embolism	5 (5)	2 (18)	1 (3)	2 (3)	0.12
Main delays					
First symptoms to ICU admission, days	9 (6–11)	10 (7–15)	9 (7–11)	9 (6–11)	0.79
Hospitalisation and ICU admission, hours	8 (0–47)	6 (0–24)	7 (0–59)	9 (0–37)	0.66
ICU admission to invasive MV, hours	19 (4–64)	61 (23–116)	31 (10–75)	11 (3–33)	0.20
Laboratory measurements					
Leukocytes, $\times 10^9$/L	9.8 (7.4–13.4)	11.2 (7.2–15.8)	8.6 (7.1–11.5)	10.8 (8.1–13.5)	0.28
Platelet count, $\times 10^9$/L	211 (152–281)	226 (125–289)	183 (145–230)	223 (162–306)	0.16
D-dimers, µg/L	1555 (982–2250)	2600 (1617–7497)	1332 (808–1753)	1555 (850–2412)	0.04
Fibrinogen, g/L	6.8 (6.1–7.9)	7.8 (7.4–8.8)	6.4 (6–7.2)	7.1 (6.1–8)	0.02
Prothrombin time, %	91 (82–100)	78 (69–84)	96 (87–100)	91 (84–100)	0.01
PaO_2/FiO_2					
Day 1	77 (54–118)	70 (44–91)	98 (74–132)	71 (56–110)	0.12
Day 3	99 (74–128)	108 (80–120)	128 (86–152)	99 (76–120)	0.051
Outcome in the ICU					
High-flow oxygen	92 (88)	10 (91)	29 (88)	53 (88)	0.99
Non-invasive ventilation	38 (37)	3 (27)	14 (42)	21 (35)	0.60
Mechanical ventilation	55 (53)	4 (36)	17 (52)	34 (57)	0.46
Vasopressor support	24 (23)	1 (9)	5 (15)	18 (30)	0.19
AKI	34 (33)	2 (18)	9 (27)	23 (38)	0.34
ECMO	5 (5)	0 (0)	1 (3)	4 (7)	0.80
Vital status					
60 Days after admission					
Alive	81 (78)	9 (82)	30 (91)	42 (70)	0.06
Deceased	23 (22)	2 (18)	3 (9)	18 (30)	

The data are expressed as median (interquartile range) or number (percentage). Groups were compared by Kruskal–Wallis or Fisher's exact test, as appropriate. No difference is statistically significant after Bonferroni correction.
AKI Acute Kidney Injury, *CT* computed tomodensitometry, *FiO2* fraction of inspired oxygen, *ICU* Intensive Care Unit, *MV* mechanical ventilation, *PaO2* partial pressure of oxygen, *SAPS* simplified acute physiology score, *SOFA* Sequential Organ Failure Assessment.
[a] Defined as haematological malignancies, active solid tumour, or having received specific anti-tumour treatment within a year, solid-organ transplant, human immunodeficiency virus, or immunosuppressants.

To the best of our knowledge, this is the first study on the characteristics of critically ill patients who are infected with V2. While there are some online data regarding this variant, they are limited and were recorded in settings where the healthcare system was saturated, there were fewer resuscitation beds/population than in France, and the variant already vastly predominated. A recent European study also showed an increased risk of being admitted to intensive care for people infected by variants of concern, compared to non-VOC cases. However, B.1.1.7 was the most frequently reported VOC and there were very little data on severe SARS-CoV-2 infection caused by the 501Y.V2 variant [5]. Our study also has limitations. The limited number of patients can reflect a lack of statistical power. Thus, infections with wild-type strain were excluded from the multivariate analysis because of their small number in the cohort. In addition, the monocentric design may have limited external validity of our findings. However, one major advantage of the study was that it could directly compare the clinical outcomes of the V2, V1, and wild-type strains due to their temporal co-existence in the region and the fact that all patients were managed by the same intensivist team in one centre who applied similar ICU/management criteria.

Table 2
Factors associated with mortality 60 days after admission in ICU for an infection with B.1.1.7 (V1) or 501Y.V2 (V2) SARS-CoV-2 strain (N = 93).

Characteristics	Alive at D60 (n = 72)	Deceased at D60 (n = 21)	p^{*}	OR [95% CI]**	p^{**}
SARS-CoV-2 strain					
B.1.1.7 (V1)	31 (41)	2 (12)	0.03	Ref.	–
501Y.V2 (V2)	45 (59)	15 (88)		5.67 [1.04–30.81]	0.04
Age (Y)	59 (49–67)	69 (63–73)	< 0.001	1.11 [1.02–1.22]	0.02
Women	26 (36)	6 (29)	0.61	0.99 [0.24–4.05]	0.99
Body mass index, kg/m^2					
< 25 kg/m^2	10 (14)	6 (30)		Ref.	–
25–30 kg/m^2	21 (30)	4 (20)	0.27	0.26 [0.04–1.74]	0.10
≥ 30 kg/m^2	41 (57)	11 (53)		0.92 [0.17–4.74]	0.39
Arterial hypertension	28 (39)	14 (67)	0.04	1.10 [0.24–4.92]	0.91
Diabetes mellitus	19 (26)	10 (48)	0.11	1.48 [0.32–6.77]	0.62
Immunodeficiency[a]	2 (3)	2 (10)	0.22	3.07 [0.12–81.56]	0.50
Cardiovascular disease	8 (11)	7 (33)	0.04	1.73 [0.35–8.56]	0.50
Chronic renal failure	2 (3)	3 (14)	0.07	2.09 [0.15–29.27]	0.59
SOFA score	5 (4–6)	7 (5–8)	0.02	1.20 [0.87–1.65]	0.28

* Wilcoxon or Fisher's exact test, as appropriate.
** Multivariate logistic regression.
[a] Defined as haematological malignancies, active solid tumour, or having received specific anti-tumour treatment within a year, solid-organ transplant, human immunodeficiency virus, or immunosuppressants.

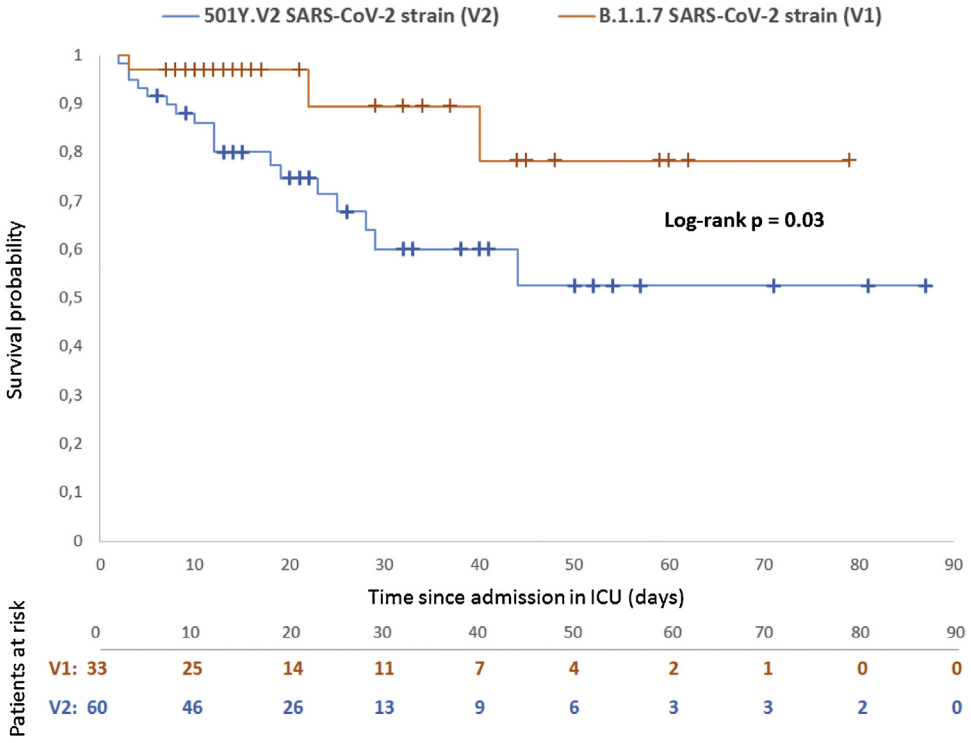

Fig. 1. Kaplan Meier survival curves for patients admitted in ICU for an infection with B.1.1.7 (V1) or 501Y.V2 (V2) SARS-CoV-2 strain (N = 93).

In summary, our preliminary data suggest that V2 variant is associated with high short-term mortality and could be more pathogenic than V1 strains.

Further studies with large cohorts are urgently needed to better understand V2 transmissibility, pathogenicity, susceptibility to treatments, and escape from natural/vaccine immunity.

Author contributions

The paper was written by GL. The statistical analysis was performed by CG. The paper was submitted to all the co-authors who made substantial contributions and agreed to submit it to *Anaesthesia Critical Care and Pain Medicine*.

Consent for publication

Not applicable.

Compliance with ethical standards

The study was carried out in accordance with the reference methodology MR-004 (N°588909v1) of the French National Commission on Information Technology and Liberties (CNIL) and was registered with ClinicalTrials.gov under identification number NCT 04430322. Patients (or their relatives if any) were notified

about the anonym use of their healthcare data via an information letter. Need for informed consent was waived as regard to the study observational design and in accordance with the French law.

Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Disclosure of interest

GL has received financial support from Pfizer, Fresenius to participate in scientific meetings during the 36 months prior to publication. All authors declare that the research was conducted in the absence of any commercial or financial relationship that could be interpreted as a potential conflict of interest.

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