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## High mortality rate in cancer patients with symptoms of COVID-19 with or without detectable SARS-COV-2 on RT-PCR

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## **Abstract (N=300)**

**Background :** Cancer patients presenting with COVID-19 have a high risk of death. In this work, predictive factors for survival in cancer patients with suspected SARS-COV-2 infection were investigated.

**Methods :** PRE-COVID-19 is a retrospective study of all 302 cancer patients presenting to this institute with a suspicion of COVID-19 from March 1st to April 25th 2020. Data were collected using a web-based tool within electronic patient record approved by the Institutional Review Board. Patient characteristics symptoms and survival were collected and compared in SARS-COV-2 RT-PCR positive and negative patients.

### **Results :**

55 of the 302 (18.2%) patients with suspected COVID-19 had detectable SARS-COV-2 with RT-PCR in nasopharyngeal samples. RT-PCR+ patients were older, had more frequently haematological malignancies, respiratory symptoms and suspected COVID-19 pneumonia of CTscan. However, respectively 38% and 20% of SARS-COV-2 RT-PCR negative patients presented similar respiratory symptoms and CT scan images. Thirty of the 302 (9.9%) patients died during the observation period, including 24 (80%) with advanced disease. At the median follow-up of 25 days after first symptoms, the death rate in RT-PCR+ and RT-PCR- patients were 21% and 10% respectively. In both groups, independent risk factors for death were male gender, KPS<60, cancer in relapse, and respiratory symptoms. Detection of SARS-COV-2 on RT-PCR was not associated with an increased death rate ( $p=0.10$ ). None of the treatment given in the previous month (including cytotoxics, PD1 Ab, anti-CD20, VEGFR2...) correlated with survival. The survival of RT-PCR positive and negative patients with respiratory symptoms and/or COVID-19 type pneumonia on CTscan was similar with a 18.4% and 19.7% death-rate at day-25. Most (22/30, 73%) cancer patients dying during this period were RT-PCR negative.

**Conclusion :** The 30-day death rate of cancer patients with or without documented SARS-COV-2 infection is poor, but the majority of deaths occur in RT-PCR negative patients.

**N=2696 words**

## **Introduction**

The death rate of COVID-19 patients is reported to be close to 2% (1). Cancer patients are a group at higher risk of serious and lethal complications of COVID-19 (2-5). The 30-days survival of patients with cancer presenting with documented COVID-19 has been reported to be 60% to 70% in recent series (2-5). These results were reported in particular from large oncology hospital in China, and were compared with patients with COVID-19 without cancer. Variability in death rates has been reported across countries and within countries possibly related to differences in screening strategies but also different population susceptibility (6-10).

The mechanisms by which the associated condition of cancer influences the risk of death to COVID-19 remains unclear. Whether this is related to the age group of cancer patients, coexisting causes (tobacco, comorbidities ...), to cancer staging, or to cancer treatment recently applied is not clear. Identifying the characteristics of cancer patients with COVID-19 at risk of a severe complication, or death would be useful to propose specific preventive measures and to adapt clinical trials.

The number of cancer patients affected with COVID is possibly underestimated. The sensitivity of RT-PCR diagnostic tests for COVID-19 ranges from 37% to 55% according to published evidence for patients with typical clinical presentation of COVID-19 (11-13). Repeated testing may increase improve detection rate in patients with initial negative SARS-COV-2 RT-PCR (12).

It is therefore important to further analyze the clinical presentation and outcome of cancer patients presenting with suspicion of COVID-19 to identify predictive factors for unfavorable outcome.

In this study (named PRE-ONCOVID-19) was investigated the survival of the exhaustive cohort of 302 patients presenting with clinical suspicion of COVID-19 consulting in a comprehensive cancer center and tested for the presence of the virus using a RT-PCR diagnostic test. The RT-PCR positive and negative subgroups were compared. Cancer patients with documented COVID-19 were found at high risk of death after diagnosis, but cancer patients without documented SARS-COV-2 infection presenting with similar symptoms were also at high risk of death. The latter subgroup represented the majority of patients succumbing during this period suggesting an important underdiagnosis of the SARS-COV-2 infection in cancer patients.

## **Patients material and methods**

### **Objectives**

The objective of the PRE-ONCOVID-19 study was to describe the clinical characteristics and survival of cancer patients presenting with COVID-19 symptoms, comparing 1) patients with documented SARS-COV-2 by RT-PCR, 2) patients with negative SARS-COV-2 RT-PCR test.

### **Study design**

PRE-ONCOVID-19 is a retrospective study of cancer patients presenting to the Comprehensive Cancer Center of Lyon (Centre Leon Berard, CLB), with a suspicion of COVID-19 from March 1st to April 15th 2020. Patient cases were collected using a web based tool enabling the collection of clinical information integrated to the electronic patient record, after Institutional Review Board approval. Patients not agreeing for the use of their clinical data for an academic study, were excluded, according to the national and European laws. The study was approved by the Institutional review board of the Centre Leon Berard on 12 March of 2020.

### **Patients**

The inclusion criteria were : an histological diagnostic of cancer, and the prescription of a diagnostic test of SARS-COV-2 with RT-PCR on a nasopharyngeal sample from March 1st 2020 to April 15th. For SARS-COV-2 RT-PCR, the cobas® SARS-CoV-2 Test (Roche , Neuilly, France) was used, exploring ORF1/a, & the Pan SARS gene E. Cancer patients presenting with clinical symptoms of COVID-19, fever and/or dry cough and/or dyspnea and/or dysgeusia anosmia and/or diarrhea, and/or suspect images on CT scan with or without a contact with a COVID-19-suspected or demonstrated contact person were included in this study. The median follow-up of the present series is 25 days.

### **Clinical definition of a group of patients with respiratory symptoms**

We identified a group of patients with respiratory symptoms suspect of COVID-19 which was defined as patients presenting with at least 2 of the 3 following symptoms : fever, dry cough, dyspnea. The observation period was from March 1st to April 25th. SARS-COV-2 RT-PCR positive and negative patients were compared, for demographics, cancer presentation, cancer characteristics, cancer treatment, clinical, radiological or biological symptoms of COVID-19 and survival.

### **Data collected in this study**

The following data were collected retrospectively : demographic characteristics (age, weight, body mass index, gender,...), cancer characteristics (histotypes, stage, relapse), the clinical presentation at the time of COVID-19 suspicion (Karnofski performance status [KPS], fever, dyspnea, cough, diarrhea, O2 requirement, CNS symptoms, vascular symptoms), presence of characteristic COVID-19 images on CT scan when performed, a selected set of biological analysis at the time of the infectious event (CRP, lymphocyte counts,..), previous cancer treatments in the last month, patient outcome (survival), comorbidities (COPD, hypertension, diabetes) in the electronic patient records. As benchmark, the comorbidities reported in the population of 43171 cancer patients in the CLB since 01/01/2015 are: COPD : 2541 (5.8%), hypertension : N=11204 (25.9%), diabetes : N=8514 (19.7%). Several additional biological factors not systematically collected were available in less than 15% of the patients ((D-Dimers, troponine, CPK) and for LDH in 35% of the patients and therefore not analyzed in this series.

Because neutrophil counts are strongly influenced by recent (<1 month) cytotoxic treatments (administered in N=137, 45% of the patients in this series), we used absolute lymphocyte counts and not neutrophil/lymphocyte ratio in this work.

### **Statistical analysis**

The distribution of risk factors or clinical characteristics were analyzed using the Chi square test, Fisher exact test, Mann-Whitney U test. The Bonferroni correction was used for multiple Chi square testing. Survival were plotted from the date of first symptoms to the date of death or to the date of last news if alive at the time of the analysis (April 25<sup>th</sup>, 2020). Survival was plotted according to the inverse Kaplan-Meier method, and groups were compared using the logrank test. Risk of death was evaluated using Cox proportional hazard model in univariate and then multivariate analysis. Backward selection procedure was used to determine the final model by removing non-significant variables ( $p>0.10$ ) one at a time. All statistical analyses will be performed using SPSS 23.0 software SPSS (IBM, Paris, France).

## Results

### Clinical characteristics of 302 cancer patients consulting for a suspicion of COVID-19 (Table 1)

As shown on Table 1, only 55 of 302 (18.2%) patients consulting for suspicion of COVID-19 had detectable SARS-COV-2 with RT-PCR on nasopharyngeal samples. SARS-COV-2 RT-PCR+ patients were older, had more frequently haematological malignancies, respiratory symptoms, diarrhea, and anosmia/ageusia, as well as suspected COVID-19 pneumonia of CT scan (Table 1). No single solid tumor subtypes were over-represented in the SARS-COV-2 RT-PCR+ subgroup (Table 1, legend). Present tobacco use (N=35, 11.6%), former tobacco use (N=61, 20.2%), report of COPD (N=26, 8.6%), diabetes (N=55, 18.2%), hypertension (N=79, 26.2%) in the electronic patient records were not significantly different between the SARS-COV-2 RT-PCR positive and negative subgroups. Recent cancer treatments (any, cytotoxics, PD1 Ab, anti-CD20, mTOR inhibitors, antiangiogenic tyrosine kinase inhibitors) were not different between the 2 groups (Table 2). However, 94 of 247 (38%) RT-PCR negative patients at the date of symptoms also had COVID-19 respiratory symptoms (defined as at least 2 of the following : fever, dry cough, dyspnea), and 32 of the 247 (20%) had characteristic CT scan images of COVID-19 pneumonia. The majority of patients in both subgroups were lymphopenic : 91 (33.5%) had deep lymphopenia <700/ $\mu$ L at the time of the infection. Similarly, both subgroups of patients had major inflammatory syndrome with a median CRP level of 96 mg/L at the date of RT-PCR, and over 16% of patients with CRP levels above 200mg/L.

### Survival of RT-PCR positive and negative cancer patients

Figure 1 shows the survival of SARS-COV-2 RT-PCR+ and RT-PCR- patients in the observation period between march 1st and April 25th. Eight of the 55 RT-PCR+ patients and 22 of the 147 RT-PCR- patients had died at the time of the analysis. With a median follow-up of 25 days, the death rates of RT-PCR positive and negative patients 25 days after the first symptoms were respectively 21% and 10%, and were not significantly different. Both the RT-PCR negative and positive groups had therefore a high death rate. None of the 302 patients of this series have received azithromycine, chloroquine, lopinavir/ritonavir, or remdesivir. One patient each received GNS561 (a chloroquin analog) and tocilizumab as part of an ongoing randomized clinical trial s standard treatment (Immunoncovid-20, NCT04333914).

The majority (24/30,80%) of cancer patients who died in this observation period had metastatic disease, both in the RT-PCR+ and RT-PCR- patients. Five patients had febrile neutropenia and none died (not shown). Present or past tobacco use, body mass index, histological subtype of the solid tumor, haematological malignancies, smoking history, comorbidities as described above were not correlated to the risk of death in these series (not shown). The administration of any cancer treatment in the month prior to the date of the first symptoms was not associated to an increased risk of death. Treatment with cytotoxics, anti CD20, anti-PD1/PDL1, mTOR inhibitors, or antiangiogenic tyrosine kinase inhibitors were not associated with an increased risk of death, neither in the SARS-COV-2 RT-PCR+ nor in the RT-PCR- subgroups (Table 2).

Table 3 shows parameters associated with an increased risk of death in the whole series and in the two SARS-COV-2 RT-PCR+ and RT-PCR- subgroups. Both in the RT-PCR positive and negative groups (Table 3), significant risk factors for death in univariate and multivariate analysis. were male gender,

KPS<60, treatment at relapse relapse, and respiratory symptoms (defined as at least 2 of the 3 : fever, dry cough, dyspnea, see patients and methods).

The multivariate analysis of risk factors for death identified these clinical parameters as well as lymphopenia <700/ $\mu$ L as independent risk factors for death, both in the overall population and in the SARS-COV-2 RT-PCR negative population (Table 3). A multivariate analysis was not performed in the SARS-COV-2 RT-PCR positive population given the limited sample.

Importantly, the presence of a SARS-COV-2 RT-PCR positive test was not significantly correlated to the risk of death in the overall population in univariate or multivariate analysis.

In view of these observations, we compared the survival of patients with positive and negative SARS-COV-2 RT-PCR presenting with respiratory symptoms (defined above in patients in methods, i.e. at least 2 of the following symptoms fever, dry cough, dyspnea) and/or CT scan images of COVID-19 pneumonia to that of the remaining patients. As shown of figure 2, the survival of RT-PCR positive and negative patients with respiratory symptoms and/or COVID-19 pneumonia at entry was worse than than of other patients. They were also similar in the SARS-COV-2 RT-PCR negative and positive subgroups with 18.4% and 19.7% death rate at day-25 after the initial symptoms (Figure 2). Most of the patients who succumbed during the observation period (22/30, 73%) were negative for SARS-COV-2 on RT-PCR.

## Discussion

Since January 2020, COVID-19 epidemic has resulted in a very large number of deaths worldwide, in particular in frail patient populations (1-10). The population of cancer patients has been reported to be particularly at risk of early death during COVID-19, with 30-days death-rates up to 39% in the initial report, vs 2.3% in the general population (2-5). Since then, additional series confirmed a high risk of death in cancer patients, which represents one of the highest risk population along with elderly patients, patients with overweight, diabetes, hypertensive disease and other associated conditions (1-10). This death rate of cancer patients is higher to that observed in large series of cancer patient consulting in emergency reported from this and other institutions, most often <5% (14-19). This death rate is also higher than that reported for seasonal influenza in large historical series (9%) and close to that reported with H1N1 (16%) (20,21).

The description of COVID-19 mortality is further complexified by the limited sensitivity of the diagnostic tests (11-13, 22). Biological diagnostic tests of COVID-19 are based on the detection of the virus using RT-PCR from biological (nasopharyngeal samples) or on the detection of specific antibodies (11-13,22). Both types of tests have limits in sensitivity, leading to false negative testing in a significant proportion of patients, even in the acute phase of the disease. For RT-PCR, the sensitivity has been reported to be inferior to 40% for the first testing, increasing up to 50% on repeated testing (12). A large proportion of patients with COVID-19 are therefore not detected by this test and clinical as well as CT scans symptoms are important to identify COVID-19 patients. Serological test also lack sensitivity, in particular in cancer patients (22).

The objective of the present PRE-ONCOVID-19 study was to analyze the characteristics, symptoms and outcome of the exhaustive population of cancer patients presenting with clinical or radiological symptoms of COVID-19 in this comprehensive cancer center, from March 1st to April 25th. This study served as the first step to build the prospective multicenter national prospective study open since April 2020 (ONCOVID-19, NCT04363632) investigating in a multicentric setting and in more details the presentation and outcome of cancer patient with documented or suspected COVID-19.

The results obtained in the PRE-ONCOVID-19 study show that only a minority, 18.2% (55/302) cancer patients presenting with clinical symptoms of COVID-19 had demonstrated SARS-COV-2 with RT-PCR performed on nasopharyngeal samples. RT-PCR+ patients were slightly older, more frequently affected with haematological malignancies, and frequently presenting with clinical respiratory symptoms, anosmia/ageusia, diarrhea and COVID-19 suspect images on CTscan, but these symptoms were also observed in a large proportion of RT-PCR- patients: close to 40% of patients presented with respiratory symptoms and/or CT scan images of COVID-19. Comorbidities (smoking history, obesity, COPD, diabetes, hypertension) were similar in RT-PCR+ and negative patients in the present series.

The biological characteristics of the RT-PCR+ and RT-PCR- patients were also similar: both populations presented similar major lymphopenia and a major inflammatory syndrome with increased CRP levels, an accurate surrogate of circulating IL-6 levels (22-24) reported to be increased in severe COVID-19 (25,26).

The majority (24/30) of cancer patients who died, in both groups, had a cancer in relapse. This parameter was retained in the multivariate analysis as a risk factor for death with a high hazard ratio in the whole series and in the 2 subgroups, while comorbidities, of SARS-COV-2 detection on RT-PCR were

not. Indeed, the risk of death of SARS-COV-2 RT-PCR positive and negative patients was not found significantly different in this series in univariate or in multivariate analysis. It was high in both subgroups, close to that reported in previous studies for the SARS-COV-2 RT-PCR+ subgroup (2-5). It was also found to be high (10% at 30 days) for SARS-COV-2 RT-PCR negative patients, higher than that of COVID-19 patients in general (1), and also higher than expected from large series of patients with cancer emergencies from the same and other institutions (14-19). It was conversely close to the mortality reported in cancer patients with seasonal influenza, and H1N1 (20,21).

Extreme lymphopenia and increased inflammatory syndrome, as evidenced by high CRP levels, are well known risk factors for early death in cancer (23-25). Still, the death rate of SARS-COV-2 RT-PCR negative cancer patients is unusually high in this series. Actually, 22 (73%) of the 30 deaths observed occurred in cancer patients with respiratory symptoms without detected SARS-COV-2 on RT-PCR. These observations strongly suggest an underdiagnosis of COVID-19 in this population of cancer patients and a major underestimation of SARS-COV-2 contribution as a cause of death in cancer patients. The management of cancer patients with febrile respiratory symptoms in this period of epidemic should therefore be particularly careful even in the absence of SARS-COV-2 detection. Dedicated clinical trials for this patient population are ongoing, testing immunotherapies, chloroquine analogs, or anti-IL-6 (Immunoncovid-20, NCT04333914).

In conclusion, this retrospective series of cancer patients presenting with suspicion of COVID-19 indicates that the death rate at 30 days after diagnosis is high both in patients with and without documented SARS-COV-2 on RTPCR, the later group representing 80% of patients. This subgroup of cancer patients presenting with COVID-19 symptoms without documented SARS-COV-2 gathers also 73%, of the observed deaths at 30 days. Specific therapeutic procedures suggested to improve COVID-19 patient survival, eg anti-IL-6 Ab (23,25,27,28), chloroquine analogs (29), remdesivir (30), should be investigated also in this SARS-COV-2 negative cancer patient population presenting with severe symptoms suggestive of COVID-19.

## **Legends of the tables and figures :**

### **Table 1 : Characteristics of the patients**

Solid tumors : breast adenocarcinoma (N=42, 13.9%), colorectal adenocarcinoma ( N=18, 5.9%) ; soft tissue sarcomas (N=15, 5.0%) ; Renal cell carcinoma (N=12, 4.0%) ; Pancreas (N=10, 3.3%) ; uterine (N=9, 3.0%) ; Bone ( N=7, 2.3%) ; Peritoneal, oesophagus, adrenal (each N=4, 1.3%) ; Anal carcinoma, ovarian adeno carcinoma, prostate adenocarcinoma, testis adenocarcinoma, Glioma (each N=3, 1.0%) ; Duodenum , parotid, mxillary sinus, supraglottis, thymoma, bladder carcinoma , CUP (each, N=2, 0.7%). All other cancer types were N=1 (0.3%).

**Figure 1 : Survival of SARS-COV-2 RT-PCR positive and negative cancer patients with a suspected COVID-19.**

**Figure 2: Survival of cancer patients consulting for suspected COVID-19 with or without respiratory symptoms.**

Patients with respiratory symptoms were defined as patients with at least 2 of the 3 following clinical symptoms (fever, dyspnea, dry cough) and/or typical images of COVID-19 pneumonia on CT-scan. A : all patients, B : RT-CPR+ patients, C : RT-PCR negative patients.

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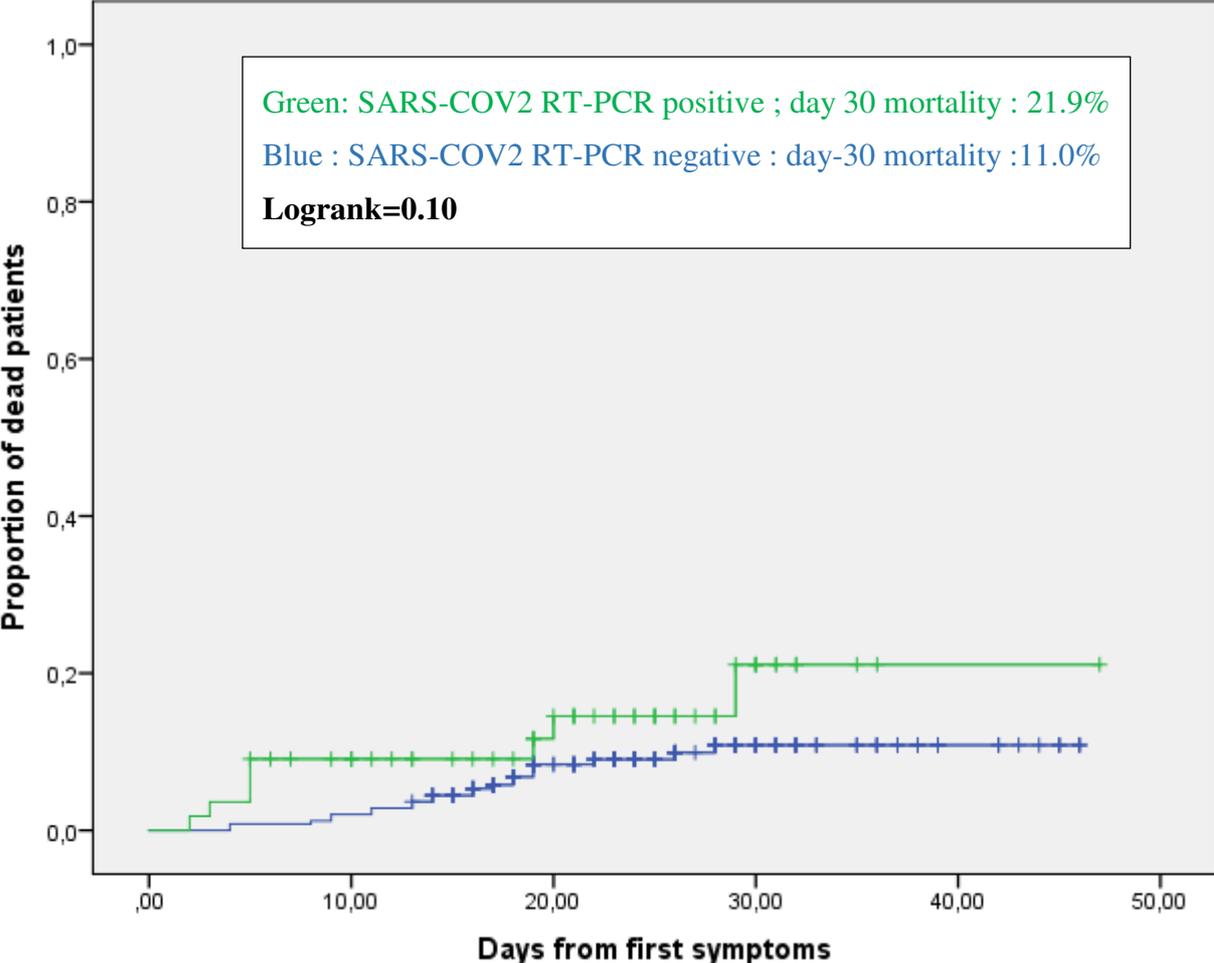
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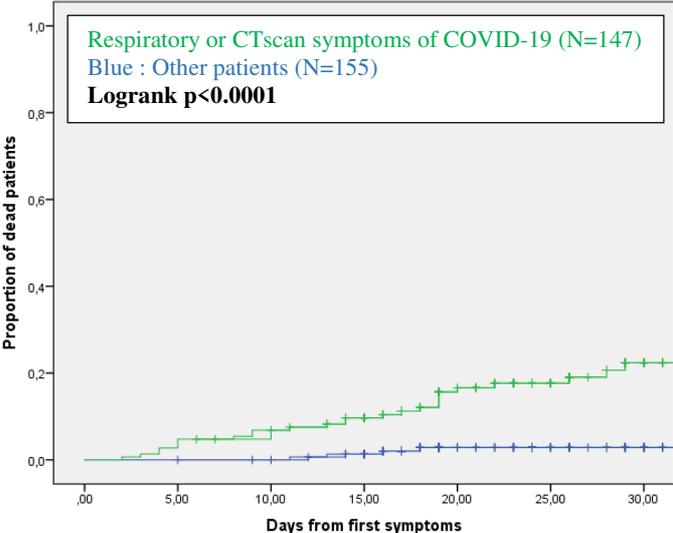
**Figure 1 : Survival of SARS-COV2 RT-PCR positive and negative cancer patients with a suspected COVID-19 infection**



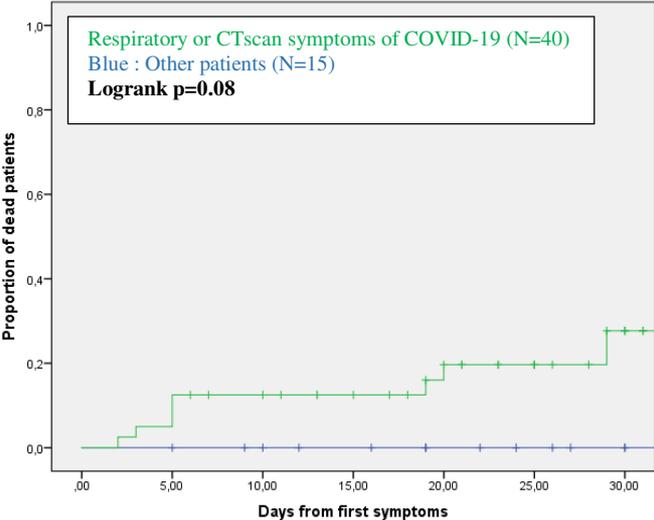
N of observations	55	45	30	12	1
N of observations	247	241	151	177	10

**Figure 2: Survival of cancer patients consulting for suspected COVID-19 with or without respiratory symptoms**

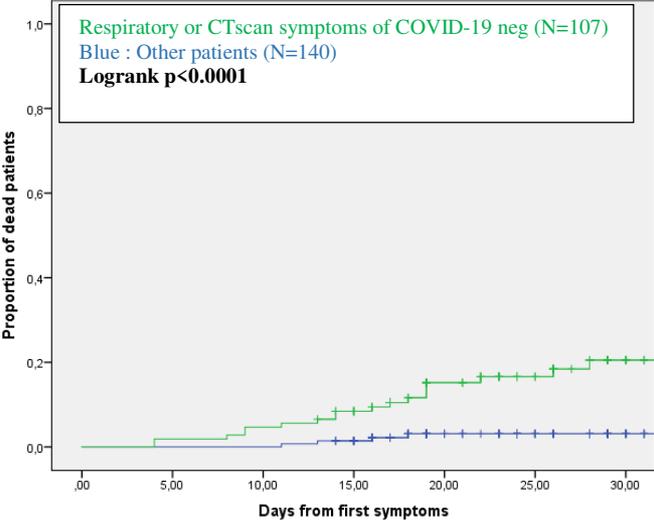
**A : All patients**



**B : SARS-COV2 RT-PCR+ cancer patients with or without clinical/radiological symptoms of COVID-19**



**C : SARS-COV2 RT-PCR- cancer patients with or without clinical/radiological symptoms of COVID-19**



**Table 1 : Characteristics of the patients**

Characteristics	All (N,%)	SARS-COV2 RT-PCR		p
		Negative (n, %)	Positive (n, %)	
<b>ALL</b>	<b>302 (100%)</b>	<b>247 (81.8%)</b>	<b>55 (18.2%)</b>	
Female	158 (52.3%)	129 (52.2%)	29(52.7%)	
Male	144 (47.7%)	118 (47.8%)	(47.3%)	0.93
<b>Age (mean, SE)</b>	<b>58.2 (1.1)</b>	<b>56.9 (1.2)</b>	<b>63.8 (2.2)</b>	<b>0.006</b>
>60	179 (59.3%)	139 (56.3%)	40 (72.7%)	<b>0.02</b>
<b>Cancer type</b>				
<i>Solid tumors*</i>	234 (77.5%)	199 (80.6%)	35 (63.6%)	
<b>Haematological</b>	<b>68 (22.5%)</b>	<b>48 (19.4%)</b>	<b>20(36.4%)</b>	<b>0.007</b>
<i>Lung</i>	42 (13.9%)	35 (14.2%)	7 (12.7%)	0.78
<b>KPS (mean, SE)</b>	69.8 (1.1)	69.1 (1.2)	72.9 (2.8)	0.15
KPS<60	114 (37.7%)	97 (39.3%)	17 (30.9%)	0.25
<b>BMI (mean, SE)</b>	24.3 (0.3)	24.2 (0.34)	24.7 (0.58)	0.43
BMI>30	120 (39.7%)	100 (40.5%)	20 (36.4%)	0.57
<b>Metastatic disease</b>	161 (53.3%)	132 (53.4%)	29 (52.7%)	0.92
<b>Relapsed disease</b>	177 (58.8%)	146 (59.1%)	31 (56.4%)	0.71
<b>Cancer treatment&lt;1 month</b>	<b>194 (64.2%)</b>	<b>165(66.8%)</b>	<b>29(52.7%)</b>	<b>0.049</b>
<b>Symptoms at entry</b>				
Fever	191 (63.7%)	150 (61.2%)	41 (74.5%)	0.06
<b>Cough</b>	<b>135 (45%)</b>	<b>96 (39.2%)</b>	<b>39 (70.9%)</b>	<b>0.000</b>
Dyspnea	94 (31.4%)	75 (30.6%)	19 (35.2%)	0.51
<b>2 or more of the above</b>	<b>130 (43.5%)</b>	<b>94 (38.4%)</b>	<b>36 (66.7%)</b>	<b>0.000</b>
<b>Diarrhea</b>	<b>42 (14.1%)</b>	<b>30 (12.3%)</b>	<b>12 (22.6%)</b>	<b>0.05</b>
<b>Anosmia/agueusia</b>	<b>21 (7%)</b>	<b>4 (1.6%)</b>	<b>17 (30.6%)</b>	<b>0.000</b>
Neurological	7 (2.3%)	3 (1.2%)	4 (7.3%)	
<b>COVID-19 suspect on CT scan</b>	<b>59 (29.5%)</b>	<b>32 (20.0%)</b>	<b>27 (67.5%)</b>	<b>0.000</b>
<b>CRP (mean, SE)</b>	96.2 (6.4)	97.9 (6.9)	86.2 (17.3)	0.55
CRP>50	133 (54.1%)	115 (55.3%)	18 (47.4%)	0.36
CRP>200	40 (16.3%)	35 (16.8%)	5 (13.2%)	0.57
<b>Lymphocyte counts (mean, SE)</b>	1136 (45.4)	1142 (49.8)	1106 (112.1)	0,78
<700/ $\mu$ L	91 (33.5%)	78 (34.1%)	13 (30.2%)	0.57
<400/ $\mu$ L	33 (12.1%)	28 (12.2%)	5 (11.6%)	0.62

\* :See legend for the different subtypes

**Table 2 : Cancer treatment in the last 30 days and patient outcome**

	n of deaths/N of patients (%)		
	All series (N=302)	SARS-COV2 RT-PCR*	
		Negative (N=247)	Positive (N=55)
<b>N of deaths †</b>	<b>30 (10%)</b>	<b>22 (8.9%)</b>	<b>8 (14.5%)</b>
<b>Treatment</b>			
No cancer treatment	13/108 (12%)	8/82 (9.7%)	5/26 (19.2%)
Any cancer treatment	17/194 (8.8%)	14/165 (8.4%)	3/29 (10.3%)
Cytotoxics	11/137 (8.0%)	11/121 (9.1%)	0/16 (0%)
Anti-CD20	1/14 (7.1%)	0/9 (0%)	1/5 (20%)
AntiPD1/PDL1	3/26 (11.5%)	3/23 (13.0%)	0/3 (0%)
Antiproteasomes	1/8 (12.5%)	1/7 (14.2%)	0/1 (0%)
Anti-HER2	0/12 (0%)	0/10 (0%)	0/2 (0%)
Everolimus (mTORi)	0/4	0/4 (0%)	0
Antiangiogenic TKI	3/18 (16.6%)	2/12 (16.6%)	1/6 (16.6%)

\* : Rates of SARS-COV-2 RT-PCR positivity were not significantly different for any of the treatment categories after correction for the number of tests performed (n=8, significant p value of  $p > 0.00625$ ) : all p values were above 0.04 using the Chi2 test.).

† : Death rates were not significantly different for any of the subgroups of treatments after correction for the number of tests performed (n=8, significant p value of  $p > 0.00625$ ) : all p values were above 0.15 using the Chi2 test.

**Table 3: Prognostic factors for survival**

	N	Deaths N (%)	Univariate analysis		Multivariate analysis	
			HR (95%CI)	p	HR (95%CI)	p
<b>All patients</b>	<b>302 (100%)</b>	<b>30 (10%)</b>				
Age>60	179	22 (12,2%)	2,01 (1,21-2,81)	0,083		
<b>Male gender</b>	<b>144</b>	<b>21 (14,5%)</b>	<b>2,66 (1,90-3,42)</b>	<b>0,01</b>	<b>2,75 (1,91-3,59)</b>	<b>0,019</b>
<b>KPS&lt;60</b>	<b>114</b>	<b>20 (17,5%)</b>	<b>9,01 (8,07-9,95)</b>	<b>&lt;0,001</b>	<b>4,87 (3,87-5,87)</b>	<b>0,002</b>
<b>Relapsing cancer</b>	<b>177</b>	<b>27 (15,2%)</b>	<b>6,81 (5,63-7,99)</b>	<b>&lt;0,001</b>	<b>3,05 (1,83-4,27)</b>	<b>0,073</b>
<b>Fever &amp; respiratory symptoms</b>	<b>130</b>	<b>25 (19,2%)</b>	<b>6,90 (5,94-7,86)</b>	<b>&lt;0,001</b>	<b>5,09 (4,11-6,07)</b>	<b>0,001</b>
Lung cancer	42	8 (19,0%)	2,38 (1,58-3,18)	0,03		
Covid-19 suspect CT Scan	59	9 (15,2%)	2,55 (1,63-3,47)	0,051		
SARS-COV2 RT-PCR+	55	8 (14,5%)	1,92 (1,12-2,72)	0,1		
CRP>50	133	22 (16,5%)	3,13 (2,23-4,03)	0,009		
<b>Ly&lt;700/μL</b>	<b>91</b>	<b>18 (19,7%)</b>	<b>4,84 (4,02-5,66)</b>	<b>&lt;0,001</b>	<b>3,05 (2,19-3,91)</b>	<b>0,05</b>
<b>SARS-COV2 RT-PCR + pts</b>	<b>55 (100%)</b>	<b>8 (14%)</b>				
<b>Age&gt;60</b>	<b>40</b>	<b>8 (20%)</b>	<b>33,9(27,4-40,5)</b>	<b>0,026</b>		
<b>Male gender</b>	<b>26</b>	<b>7 (26,9%)</b>	<b>8,19 (6,09-10,3)</b>	<b>0,014</b>		
<b>KPS&lt;60</b>	<b>17</b>	<b>6 (35,2%)</b>	<b>7,7 (6,09-9,31)</b>	<b>0,005</b>		
<b>Fever &amp; respiratory symptoms</b>	<b>36</b>	<b>8 (22,2%)</b>	<b>36,9(30,5-43,3)</b>	<b>0,017</b>		
Lung cancer	7	3 (42,9%)	4,69 (3,24-6,14)	0,16	<b>ND</b>	
Covid-19 suspect CT Scan	27	7 (25,9%)	0,89 (-0,64-2,42)	0,072		
Relapsing cancer	31	7 (22,5%)	5,29 (3,19-7,39)	0,061		
<b>CRP&gt;50</b>	<b>18</b>	<b>6 (66,6%)</b>	<b>6,87 (4,75-8,99)</b>	<b>0,039</b>		
<b>Ly&lt;700/μL</b>	<b>13</b>	<b>3 (23,1%)</b>	<b>8,98 (6,71-11,3)</b>	<b>0,037</b>		
<b>SARS-COV2 RT-PCR neg. pts</b>	<b>247</b>	<b>22 (8%)</b>				
Age>60	139	14 (10.1%)	1,4 (0,54-2,26)	0,43		
Male gender	118	14 (11.9%)	1,97 (1,11-2,83)	0,11		
<b>KPS&lt;60</b>	<b>97</b>	<b>19 (19.6%)</b>	<b>10,6 (9,38-11,82)</b>	<b>&lt;0,001</b>	<b>6,64 (5,41-7,87)</b>	<b>0,003</b>
<b>Relapsing cancer</b>	<b>146</b>	<b>20 (13.7%)</b>	<b>7,5 (6,05-8,95)</b>	<b>&lt;0,001</b>	<b>4,26 (2,79-5,73)</b>	<b>0,053</b>
<b>Fever &amp; respiratory symptoms</b>	<b>94</b>	<b>17 (18.1%)</b>	<b>5,78 (4,78-6,78)</b>	<b>&lt;0,001</b>	<b>4,9 (3,90-5,90)</b>	<b>0,002</b>
Covid-19 suspect CT Scan	32	2 (6.2%)	0,89 (-0,64-2,42)	0,87		
CRP>50	115	16 (13.9%)	2,67 (1,67-3,67)	0,05		
<b>Ly&lt;700/μL</b>	<b>78</b>	<b>15 (19.2%)</b>	<b>4,39 (3,49-5,29)</b>	<b>0,001</b>	<b>2,16 (1,24-3,08)</b>	<b>0,09</b>