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## Study of the SARS-CoV-2-specific immune T-cell responses in COVID-19-positive cancer patients

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34 **Abstract**

35 **Background:** Cancer patients are considered as highly vulnerable to COVID-19 pandemic. However,  
36 delaying cancer specific therapies could have a deleterious effect on survival. The potential suppressive effects  
37 of chemotherapies or cancer-related microenvironment raised the question on how cancer patients' immune  
38 system responds to SARS-CoV-2 virus.

39 **Methods:** We have started a prospective monocentric trial entitled COV-CREM (NCT04365322) on  
40 April 2020. The primary trial objective was to assess specific immune response's intensity and diversity to  
41 SARS-CoV-2 for infected patients.

42 **Results:** In this study, we showed that cancer patients (28 solid tumors, 11 hematological malignancies)  
43 exposed to SARS-CoV-2 produced high rate of specific antibodies, as observed in patients without cancer  
44 history (n=29). However, our results highlight a lack in the generation of T-cell responses against CoV-N, M and  
45 S proteins from SARS-CoV-2 virus, suggesting that cancer patients failed to mount a protective T-cell  
46 immunity. Nevertheless, SARS-CoV-2 infection did not impair established immune memory since specific  
47 responses against common viruses was not hampered in cancer patients.

48 **Conclusion:** Given the severity and the unknown evolution of the ongoing COVID-19 pandemic, it is  
49 of fundamental importance to integrate cancer patients in vaccination programs.

50

51 **Keywords :** SARS-CoV-2 infection, cancer patients, immune T cell response, SARS-CoV-2 antibodies.

52 **1. Introduction**

53 Today's fight against the SARS-CoV-2 virus generates a scientific emulation that brings together researchers  
54 from all horizons. Older age and medical comorbidities are the main risk factors for severe outcomes and higher  
55 mortality from COVID-19 infection [1]. This is why cancer patients are considered as highly vulnerable [2,3].  
56 Comorbidities and active cancer are the major factors for high risk COVID-19-related severe events [4–6]. In a  
57 SARS-CoV context, T-cells are critical in virus clearance by eliminating virus-infected cells both in mice models  
58 and human [7–9]. SARS-CoV viruses are composed of structural proteins named N (nucleocapsid), M  
59 (membrane), E (envelope) and S (spike). Recently Grifoni et al. reported the presence of SARS-CoV-2 specific  
60 T-cells, using peptides derived from these structural proteins, in convalescent patients who presented a mild  
61 illness form [9]. The supposed vulnerability of cancer patients in COVID-19 pandemic raised the questions of  
62 how the immune system of these patients responds against the SARS-CoV-2. However, delaying treatment is not  
63 recommended during COVID-19 pandemic. Cancer patients must receive antitumor treatment under a vigorous  
64 SARS-CoV-2 screening. A growing evidence sustains the rational for the development of vaccine against SARS-  
65 CoV-2 [7,8,10]. Thus, it is critical to understand how the immune system of the supposedly vulnerable cancer  
66 patients would respond against the SARS-CoV-2 to anticipate the impact of a possible vaccine on this patient.

67

68 **2. Material and Methods**

69 *2.1 Patients*

70 We have started a prospective monocentric trial entitled COV-CREM (NCT04365322) on April 2020.  
71 All patients were enrolled after the signature of informed consent in accordance with the French regulation.  
72 Three cohorts of patients were enrolled: i) patients with mild illness COVID-19 infection without cancer, whose  
73 clinical parameters have been described elsewhere [11] ii) patients with solid tumors, iii) patients with  
74 hematological malignancies. The analyzed population was diagnosed with COVID-19 between March 10 and  
75 May 20. Patients with cancers were included if they presented a COVID-19 infection diagnosed based on RT-  
76 PCR performed on nasopharyngeal swab or positive serology. The primary trial objective was to assess specific  
77 immune response's intensity and diversity to SARS-CoV-2 for infected patients. In this study, we presented the  
78 results of 28 patients with solid tumors and 11 patients with hematological malignancies. Results are  
79 comparatively analyzed against immune analyses performed in healthy donor's samples and patients treated for  
80 mild illness COVID-19 infection without cancer history [11]. A detailed description of the methods can be found  
81 in the supplementary methods.

82

83 *2.2 Immune responses analysis*

84 Peripheral blood mononuclear cells (PBMC) from patients and healthy donors were isolated by density  
85 centrifugation on Ficoll gradient (Eurobio). We assessed spontaneous T-cell responses against SARS-CoV-2 by  
86 using IFN $\gamma$  ELISpot assay. Humoral responses was assessed by using ELISA assay to detect IgG antibodies to  
87 SARS-CoV-2. A detailed description of the laboratory analysis methods can be found in the supplementary  
88 methods.

89 *2.3 Statistical analysis*

90 Statistical analyses were performed using GraphPad Prism 6 software (San Diego, CA). The level of significance  
91 was set at  $p < 0.05$  for all tests (\*  $p \leq 0.05$ , \*\*  $p \leq 0.01$ , \*\*\*  $p \leq 0.001$  and \*\*\*\*  $p \leq 0.0001$ ). Variables were  
92 expressed as a median and interquartile range (IQR) and tested with the Mann-Whitney U test. Variables were  
93 expressed as frequencies and tested with the Fisher's exact test.

94

95 **3. Results**

96 Cancer patients' characteristics are reported in **table 1** and **table 2**. All enrolled patients presented a  
97 mild illness form of COVID-19. The viral load detected in nasal swabs was available for 16 patients. For  
98 majority of them (88%), the viral load was high (mean 19.5 ct (15.29-36.76)). We notice that four patients were  
99 hospitalized for preventive approach. The median age was 69. When diagnosed with COVID-19, 82% had fever.  
100 At the time of infection, 61.5 % of patients had metastatic or advanced stage of cancer whom 79.2% had ongoing  
101 anticancer therapies (excluding hormonotherapy) and thirteen (68.4%) displayed a lymphopenia (lymphocyte  
102 count under 1G/L).

103 Among patients with cancers, 14 out of 28 patients with solid tumors (50.0%) and 4 out of 11 patients  
104 with hematological malignancies (36.4%) exhibited T-cell responses against at least one of the SARS-CoV-2  
105 proteins (CoV-S, CoV-M or CoV-N) (**Fig. 1A**). In line with a potential cross reactivity with previous  
106 coronavirus exposition, recognition of CoV-S, M and N proteins by T-cells was observed in respectively 33.3%,  
107 33.3% and 14.3% of the healthy donors tested (**Fig. 1B**). Furthermore, SARS-CoV-2 elicited specific immune  
108 responses against CoV-M and CoV-N in 58.6 and 65.5% of the patients without a cancer history ( $p \leq 0.05$  and  
109  $p \leq 0.01$  respectively) (**Fig. 1B, middle and right panel**). The T-cell immune responses intensity against SARS-  
110 CoV-2 proteins was investigated. No statistically significant differences were observed between the responses of  
111 patients without a cancer history and both cohorts of cancer patients. This provides evidence that immune

112 responses during SARS-CoV-2 infection does not sustain antigen memory T-cells detectable in the peripheral  
113 blood mononuclear cells. There were no significant frequency differences in CoV-S T-cell responses between  
114 patients with solid tumor (42.8%) or hematological malignancies (27.3%), patients without a cancer history  
115 (37.9%) or healthy donors (33.3%) (**Fig.1B, left panel**). Specific CoV-M and N T-cell responses frequencies  
116 tend to be lower in patients with hematological malignancies compared to patients without a cancer history  
117 (27.3% vs 58.6% ( $p=0.15$ ) and 36.4% vs 65.5% ( $p=0.15$ ) for SARS-CoV-M and N respectively) (**Fig. 1B**  
118 **middle and right panel**). Specific CoV-N T-cells responses frequencies were statistically lower in patients with  
119 solid tumors compared to patients without a cancer history (35.7% vs 58.6%,  $p=0.0348$ ). The one against CoV-  
120 M tends to be lower (39.3% vs 58.6%,  $p=0.12$ ) (**Fig. 1B**). Interestingly, two cancer patients without peripheral  
121 SARS-CoV-2 specific T-cells had prolonged virus RNA detection after symptoms resolution, while no  
122 prolonged RNA production was reported in patients with specific adaptive immunity. The SARS-CoV-2 specific  
123 T-cells absence was not correlated to clinical determinants. Similarly, lymphopenia and lymphocyte subset  
124 distribution did not account for the lack of SARS-CoV-2 specific immunity (**Table 1**).

125 The other immunological issue for cancer patients is the potential risk that SARS-CoV-2 virus-mediated  
126 infection dampens pre-existing memory T-cell repertoire. To investigate this issue, we concomitantly measured  
127 the reactivity against common viruses using IFN $\gamma$  ELISpot assay. Median intensities and frequencies were  
128 similar across all patients' groups. (**Fig. 1C**). This demonstrated that recent history of COVID-19 did not hamper  
129 viral memory T-cell pool in patients with or without cancers. It suggests that the lack of SARS-CoV-2 specific  
130 T-cells is related to a weak immune adaptive response initiation rather than a global T-cell dysfunction.

131 We then analyzed the SARS-CoV-2 humoral responses. We compared the serology index between our  
132 patients' cohorts (**Fig. 1D**). The median serology index in patients without cancer history was (5.6 S/CO [IQR:  
133 2.9-6.6]) and statistically lower when compared to patients with solid tumors 6.9 S/CO [IQR: 5.0-8.3] ( $p=0.016$ ).  
134 In contrast patients with hematological malignancies had a median serology index equal to 3.25 S/CO [IQR 0.1-  
135 6.3] that was statistically lower when compared to both patients with solid tumors and without cancer history  
136 ( $p=0.0017$  and  $p=0.052$ ). A heatmap was generated, using the online Morpheus software  
137 (<https://software.broadinstitute.org/morpheus/>), to correlate all immunological parameters investigated (**Fig. 1E**).  
138 These results unravel that SARS-CoV-2 infection is associated with a lack of adaptive T-cell immunity in cancer  
139 patients. In addition, a discrepancy was unraveled, in the context of cancer history, between SARS-CoV-2  
140 seroconversion and the presence of memory T-cells.

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143 **4. Discussion**

144 To date, few studies have analyzed specific SARS-CoV-2 cellular and humoral responses in cancer  
145 patients. This study, based on patients with solid tumors treated mostly at a metastatic stage, showed a high rate  
146 of SARS-CoV-2 antibody production. The specific T-cell response frequency in cancer patients was similar to  
147 the one in healthy donors and significantly lower than the frequency in COVID-19 patients without cancer  
148 history underlying the weakness of SARS-CoV-2 immunogenicity in cancer patients. The presence of SARS-  
149 CoV-2 specific T-cells in healthy donors might be explained by the sequence homology between structural  
150 proteins from various coronavirus suggesting the existence of cross reactive memory T-cells [12,13]. Indeed,  
151 high degrees of similarities between coronaviruses and SARS-CoV-2 concerning S, M and N structural proteins  
152 have been recently described [14,15].

153 This study is intended to be descriptive but not comparative. The small cohort of cancer patients studied  
154 is heterogeneous in terms of cancer type and anticancer treatment at the time of COVID-19 infection, which  
155 make it difficult to statistically explain confounding factors of non-response. However, both cohort of patients  
156 were comparable in term of COVID-19 severity and included patients with a mild disease. The T-cell responses  
157 against common viruses (Cytomegalo-, Epstein-Barr and Flu-virus) were used as a control of memory T-cell  
158 responses. The level of T-cell responses against CEF was similar between the two cohorts excluding a possible  
159 abnormality of peripheral memory T-cells compartment. Nevertheless, the effect of previous line of anticancer  
160 treatment as well as lymphopenia at the time of the infection remain to be investigated in larger cohort of  
161 patients.

162 The impairment of adaptive immunity due to immune suppressing therapies might alter cancer patients'  
163 outcome following COVID-19. Patients with hematological malignancies have usually long lasting  
164 immunodeficiency because of the malignancy itself but also because of anti-cancer treatments such as rituximab  
165 or hematopoietic stem-cell transplantations[16]. In a first report of COVID-19 in chronic lymphocytic leukemia  
166 (CLL) patients receiving venetoclax showed a substantial adaptive immune deficiency that might lead to an  
167 impairment of T-cell responses and more COVID-19 severity in infected CLL patients [17]. The cases of severe  
168 COVID-19 have also been reported in patients treated with anti-CD20 targeted therapy supporting the impact of  
169 B-cell depletion thereby the incapacity to produce neutralizing antibodies on COVID-19 course [18,19].  
170 Nevertheless, in a recent multicentric study including 177 patients with lymphoma, active treatment and the  
171 number of prior lines did not show significant differences in mortality due to the infection [20]. Furthermore, in

172 a study including 423 cases of patients with solid tumors, the active anticancer treatment did not show a  
173 significant association with the COVID-19 severity [21]. The potential effect of immunosuppressive treatments  
174 on the severity of COVID-19 disease and outcome need futures investigations in larger cohort of patients.

175 The induction of anti-SARS-CoV-2 protective immunity by vaccine in cancer patients is an important  
176 medical need. However, the heterogeneity of SARS-CoV-2 specific-T-cell responses among cancer patients'  
177 emphasize the interest to investigate anti-SARS-CoV-2 immune responses following vaccination in this  
178 population

179 To summarize, this study raises three major concerns to be considered for further research programs: i)  
180 Adaptive T-cell immunity targeting SARS-CoV2 is weak in cancer patients compare to common viruses; ii)  
181 specific immunoglobulin monitoring is not sufficient to characterize anti-SARS-CoV-2 immunity and assays to  
182 monitor specific T-cell responses should be developed, iii) SARS-CoV-2 infection does not alter the common  
183 virus's memory T-cell responses level in cancer patients. Even if those first data need to be confirmed in a larger  
184 cohort, the present results support the promotion of specific SARS-CoV-2 vaccination programs for cancer  
185 patients given the ongoing COVID-19 pandemic severity.

186

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189

#### 190 **Conflict of interest statement**

191 The authors have no conflicts relevant to this work to declare.

192

193 Authors' contribution L. Mansi, L. Spehner, M.Kroemer had full access to all data in the study and take  
194 responsibility for the integrity of the data and accuracy of data analysis. Study concept and design: M.Kroemer,  
195 K.Bouiller, L.Mansi, L.Spehner, E. Daguindeau, C.Borg, O.Adotévi. Acquisition, analysis or interpretation of  
196 data: all authors. Drafting of the manuscript: L.Mansi, M.Kroemer, L.Spehner, C.Borg. Statistical Analysis:  
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**Figure Legend**

**Figure 1: SARS-CoV-2 specific T-cell responses were increased in COVID-19 patients without cancer history compared to COVID-19 patient with solid or hematological malignancies.**

PBMC from 21 healthy donors and COVID-19 patients without cancer history ( $n=29$ ), solid tumor ( $n=28$ ) or hematological malignancies were analyzed for SARS-CoV-2 and antiviral-specific T-cell responses by IFN $\gamma$  ELISpot assay. **A.** Frequency of patients with specific responses at least one SARS-CoV-2 proteins. **B.** Frequencies (%) of positive SARS-CoV-2 specific immune responses in healthy donors and COVID-19 patients (Mann Whitney test,  $*p>0.05$ ). **C.** Frequency (%) of positive antiviral memory CD8 T-cell responses in healthy donors and COVID-19 patients. **D.** The median serology index (S/CO) in COVID-19 patients without cancer history, solid tumor or hematological malignancies (Mann Whitney test,  $*p>0.05$ ,  $**p>0.01$ ). **E.** Heatmap showing the positivity or the negativity of the serology index, T-cell immune responses to SARS-CoV-S, M and N proteins for each patient included in the study (online Morpheus software). Healthy donors' population is represented by the color light gray, COVID-19 patients without cancer history by the color black, COVID-19 patients with solid tumor by the color blue and hematological malignancies by the color violet.

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**Table 1. Cancer patient's characteristics**

	With T cell responses		Without T cell response	
	Solid tumors (n=14)	Hematological malignancies (n=4)	Solid tumors (n=14)	Hematological malignancies (n=7)
<b>Patients characteristics n (%)</b>				
<b>Age - median (year)</b>	70	73	69	59
[Range]	[51-75]	[54-80]	[48-84]	[23-73]
< 65	4 (28.6)	1 (25.0)	6 (42.9)	4 (57.1)
65-74	8 (57.1)	2 (50.0)	5 (35.7)	3 (42.9)
>75	2 (14.3)	1 (25.0)	3 (21.4)	0 (0)
male	7 (50.0)	4 (100.0)	5 (35.7)	4 (57.1)
<b>History of cancer n (%)</b>				
<b>Metastatic or late stage</b>	9 (64.3)	1 (25.0)	12 (85.7)	2 (28.6)
<b>Active Anticancer treatment during 4 weeks before COVID infection</b>	10 (71%)	3 (75.0)	12 (85.7)	1 (50)
Chemotherapy	6 (42.9)	0 (0.0)	6 (42.9)	0 (0.0)
Chemotherapy + immunotherapy	0 (0.0)	1 (25.0)	1 (7.1)	0 (0.0)
Immunotherapy	2 (14.3)	1 (25.0)	1 (7.1)	0 (0.0)
Targeted therapy	1 (7.1)	1 (25.0)	4 (28.6)	1 (50)
Hormonotherapy	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)
<b>COVID-19 n (%)</b>				
<b>Symptomatic</b>	12 (85.7%)	4 (100.0)	14 (100.0)	7 (100.0)
<b>Diagnostic of COVID-19</b>				
PCR	8 (57.1)	4 (100.0)	11 (78.6)	7 (100.0)
PCR+ >1 month	0 (0.0)	0 (0.0)	3 (21.4)	1 (14.3)
Serology	6 (42.9)	0 (0.0)	3 (21.4)	0 (0.0)
<b>Time between COVID-19 infection and blood sample - median [range] in days</b>	70.5 [48 – 109]	76.5 [49 – 92]	62.5 [41 – 85]	81.0 [48 – 119]
<b>Immunological data</b>				
<b>PNN median (mm<sup>3</sup>)</b>	2 205	2 935	3 075	5 550
[range]	[1 370 – 5 250]	[1 410 – 5 980]	[902 – 9 000]	[900 – 35 000]
Missing	4	0	0	1
<b>LDH median (UI/I)</b>	417	199	239	444
(range)	[207 – 464]	[177 – 235]	(61 – 341)	(206 – 750)
Missing	8	1	3	3
<b>Lymphopeny at the moment of COVID-19 infection (G/L)</b>				
n (%)	3 (42.8)	2 (50.0)	9 (64.3)	2 (28.6)
Median [range]	1 340 [600-2 060]	1 505 [690-2 320]	840 [300 – 1 920]	1 300 [580 – 1 900]
Missing	7	0	0	1
<b>CD3 (%) [range]</b>				
<b>CD4 (%) [range]</b>	54.1 [26.4 – 89.4]	65 [14.7 – 94.5]	61.1 [31.7 – 87.5]	54.4 [5.2 – 91.1]
<b>CD8 (%) [range]</b>	51.3 [16.2 – 91.5]	31.1 [4.3 – 51.4]	52.2 [20.8 – 83.7]	46.7 [8.3 – 66.2]
<b>CD4/CD8 (%) [range]</b>	38.5 [7.1– 69]	58.9 [39.4 – 92.3]	35.9 [13.8 – 63.3]	48.4 [24.7 – 90.3]
<b>CD19 (%) [range]</b>	2.4 [0.3 – 12.8]	0.6 [0.04 – 1.3]	2.0 [0.4 – 5.8]	1.3 [0.09 – 2.6]

Missing	23.9 [1.5 – 58.3] 0	27.3 [1 – 87.8] 0	27.6 [2.9 – 75.1] 2	18.7 [0.1 – 59.1] 2
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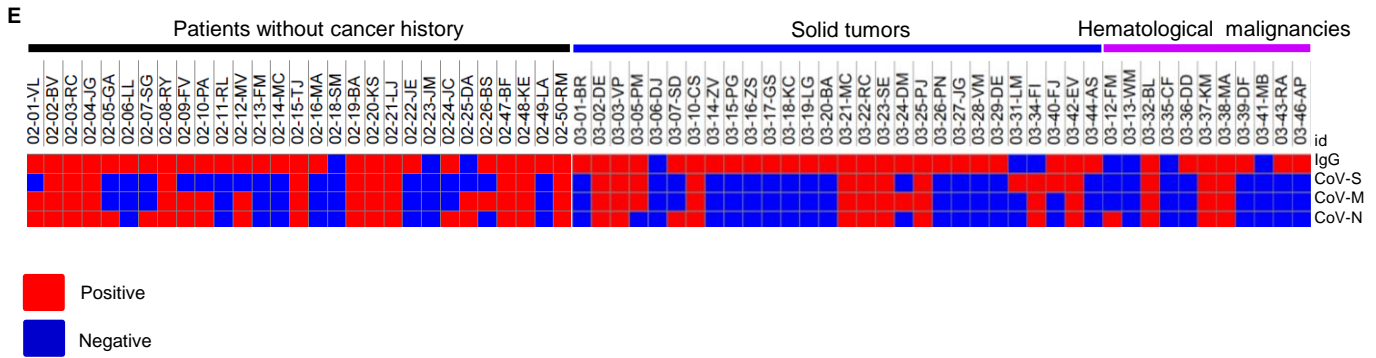
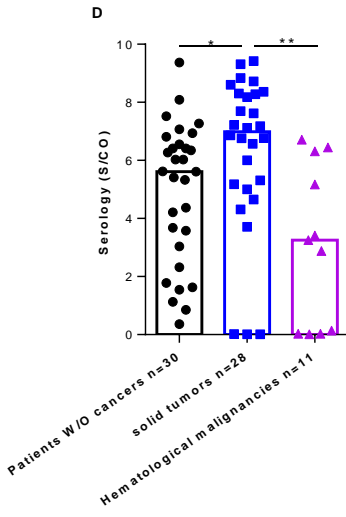
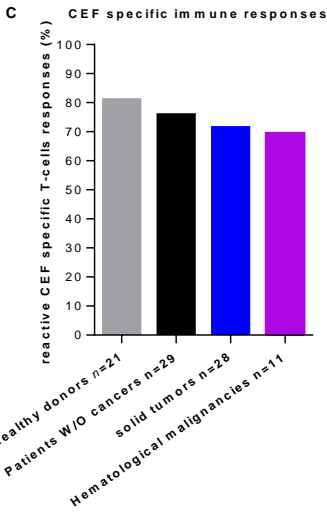
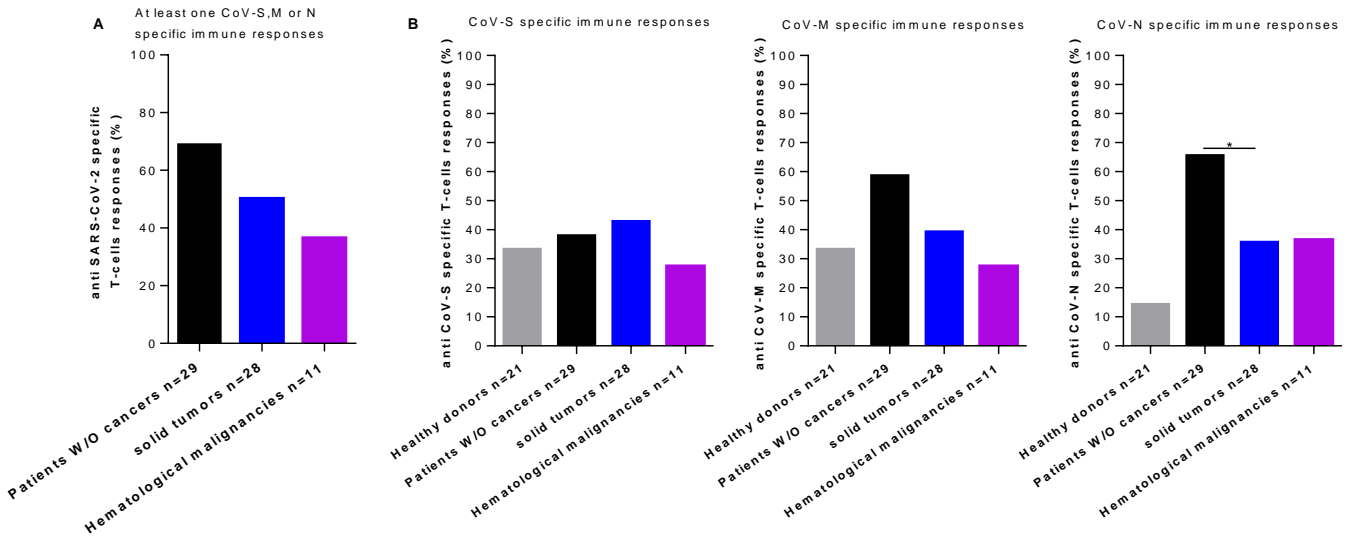
**Table 2. Clinical characteristics of individual cancer patients**

Patient number	Solid tumors														
	Sexe	Age	PS	Diabete	BMI	HTA	Other Comorbidities	Concurrent Ongoing Therapies	Cancer localisation	Metastatic Disease Y/N	Active Anti-cancer Treatment during 4 weeks before COVID Infection	Time between COVID-19 infection and blood sample in days	COVID-19 serology	At least one specific T cell response (S, M or N)	CEF specific T cell responses
03-01	M	72	1	NO	27.7	YES	NO	NO	Hepatocarcinoma	YES	Sorafenib	64,0	POS	NO	YES
03-02	F	53	0	NO	26.5	NO	NO	NO	Breast	YES	Trastuzumab Pertuzumab Hormonotherapy	72,0	POS	YES	YES
03-03	M	55	3	NO	23.8	NO	Arrhythmia	Amlodipine Cordarone Perindopril	Pulmonary	NO	Durvalumab	85,0	POS	YES	YES
03-05	F	75	1	NO	26.5	YES	NO	NO	Breast	YES	Hormonotherapy	70,0	POS	YES	YES
03-06	M	62	3	NO	24.3	YES	Arrhythmia	Sotalol Apixaban	HNC	YES	NO	54,0	NEG	NO	YES
03-07	M	69	2	NO	19.8	YES	NO	NO	HNC	YES	Methotrexate	48,0	POS	YES	YES
03-10	F	69	0	NO	24.8	NO	Dyslipidemia	Pravastatine	Colorectal	YES	FOLFOX	63,0	POS	YES	YES
03-14	F	75	1	NO	21.5	NO	NO	NO	Breast	YES	Capecitabine Lapatinib	85,0	POS	NO	YES
03-15	M	73	1	NO	18	NO	NO	NO	Pulmonary	YES	Cisplatin Pemetrexed Pembrolizumab	58,0	POS	NO	NO
03-16	F	48	1	NO	24.4	NO	NO	NO	Breast	NO	Trastuzumab	61,0	POS	NO	NO
03-17	F	74	0	NO	18.6	NO	NO	NO	Glioblastoma	YES	NO	59,0	POS	NO	YES
03-18	F	62	0	NO	22.3	NO	NO	NO	Breast	YES	Tucatinib Capecitabine Trastuzumab	85,0	POS	NO	YES
03-19	M	67	1	NO	20.5	YES	NO	NO	Stomach	YES	FOLFIRI	67,0	POS	NO	YES
03-20	F	64	1	NO	21	NO	NO	NO	Ovarian	YES	Liposomal doxorubicin	60,0	POS	NO	NO
03-21	F	57	1	NO	40	YES	NO	NO	Ovarian	YES	Carboplatin Paclitaxel	83,0	POS	YES	YES
03-22	F	71	0	NO	22	NO	NO	NO	Breast	NO	NO	91,0	POS	YES	YES
03-23	M	72	2	NO	21	NO	NO	NO	Colorectal	YES	FOLFOX Bevacizumab	71,0	POS	YES	YES

03-24	M	70	0	NO	21	NO	NO	NO	Vesical	NO	NO	81,0	POS	YES	YES
03-25	M	74	1	NO	19.8	NO	NO	NO	HNC	NO	DCF	69,0	POS	YES	NO
03-26	M	84	1	NO	22.6	NO	NO	NO	Renal	YES	Nivolumab	65,0	POS	NO	NO
03-27	F	80	0	YES	26	NO	NO	NO	Hepatocarcinoma	YES	Sorafenib	56,0	POS	NO	YES
03-28	F	62	0	NO	19.3	NO	NO	NO	Breast	NO	Docetaxel	75,0	POS	NO	NO
03-29	F	70	0	NO	31	YES	NO	NO	Breast	YES	Palbociclib Hormonotherapy	85,0	POS	NO	NO
03-31	M	75	2	NO	20	NO	Ischemia Cardiopathy - Chronic Renal Failure	Sotalol Perindopril Metformin Lercanidipine	Pulmonary	YES	NO	70,0	NEG	YES	YES
03-34	F	64	1	NO	25	NO	NO	NO	Renal	YES	Nivolumab	101,0	NEG	YES	YES
03-40	M	74	1	YES	24.7	YES	NO	NO	Prostate	YES	Cabazitaxel	89	POS	YES	NO
03-42	F	51	2	NO	20	YES	NO	NO	Sarcoma	NO	NO	109	POS	YES	YES
03-44	F	58	1	NO	19	YES	NO	Hydrochlorothiazide	Pancreas	YES	Gemcitabine	41	POS	NO	YES
<b>Hematological malignancies</b>															
Patient number	Sexe	Age	PS	Diabete	BMI	HTA	Other Comorbidities	Concurrent Ongoing Therapies	Cancer localisation	Disease stage	Active Anti-cancer Treatment during 4 weeks before COVID Infection	Time between COVID-19 infection and blood sample in months	COVID-19 serology	At least one T cell response (S, M or N)	CEF specific T cell responses
03-12	M	73	1	NO	1.72	NO	NO	NO	DLBCL	Early	R-CHOP	49	NEG	YES	YES
03-13	M	23	1	NO	2.5	NO	NO	Valaciclovir Tacrolimus Prednisone	ALL	Early	NO (allograft in october 2019)	48	NEG	NO	YES
03-32	M	80	1	NO	2	YES	NO	Sotalol	CLL	Early	R-Venetoclax	80	POS	YES	NO
03-35	F	48	2	YES	1.4	NO	Pulmonary transplantation	Tacrolimus	AML	Early	NO (Allograft in 2006)	48	NEG	NO	NO
03-36	M	54	1	NO	2	NO	NO	Tacrolimus	AML	Early	NO (Allograft in august 2019)	54	POS	NO	NO
03-37	M	54	2	NO	1.9	NO	NO	Prednisone Polyvalent Intravenous Immunoglobulin	AML	Early	NO (Allograft in 2007)	54	POS	YES	YES
03-38	M	72	1	NO	1.8	YES	Hypothyroidism	Levothyroxine	Multiple myeloma	Late	Isatuximab Pomalidomide Dexamethasone	72	POS	YES	YES

<b>03-39</b>	F	73	2	NO	1.7	NO	Stroke	Valaciclovir	AML	Late	Venetoclax	73	POS	NO	YES
<b>03-41</b>	M	67	1	NO	2.1	NO	Arrhythmia	Prednisone	Myelodysplastic syndrome	Late	NO	67	NEG	NO	YES
<b>03-43</b>	F	52	1	NO	2.2	NO	Hypothyroidism	Levothyroxine	CML	Early	Nilotinib	52	POS	NO	NO
<b>03-46</b>	M	66	1	NO	2.1	NO	NO	Valaciclovir Irbesartan	Bone marrow failure	Early	Cyclosporine	66	NEG	NO	YES

**Abbreviation:** ALL Acute Lymphocytic AML Acute Myelogenous Leukemia CLL Chronic Lymphocytic Leukemia CML Chronic Myelogenous Leukemia DCF Docetaxel Cisplatin Fluorouracile DLBC Diffuse Large B Cell Lymphoma F Female HNC Head and Neck Cancer Leukemia M Male PS Performans Status





**Figure 1: SARS-CoV-2 specific T-cell responses were increased in COVID-19 patients without cancer history compared to COVID-19 patient with solid or hematological malignancies.**

PBMC from 21 healthy donors and COVID-19 patients without cancer history ( $n=29$ ), solid tumor ( $n=28$ ) or hematological malignancies were analyzed for SARS-CoV-2 and antiviral-specific T-cell responses by IFN $\gamma$  ELISpot assay. **A.** Frequency of patients with specific responses at least one SARS-CoV-2 proteins. **B.** Frequencies (%) of positive SARS-CoV-2 specific immune responses in healthy donors and COVID-19 patients. Mann Whitney test, \* $p>0.05$ . **C.** Frequency (%) of positive antiviral memory CD8 T-cell responses in healthy donors and COVID-19 patients. **D.** The median serology index (S/CO) in COVID-19 patients without cancer history, solid tumor or hematological malignancies. Mann Whitney test, \* $p>0.05$ , \*\* $p>0.01$ . **E.** Heatmap showing the positivity or the negativity of the serology index, T-cell immune responses to SARS-CoV-S, M and N proteins for each patients included in the study (online Morpheus software). Healthy donors' population is represented by light gray points, COVID-19 patients without cancer history by black points, COVID-19 patients with solid tumor by blue points and hematological malignancies by violet points.