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Journal Pre-proof

Seroconversion in patients with cancer and oncology healthcare workers infected by SARS-CoV-2

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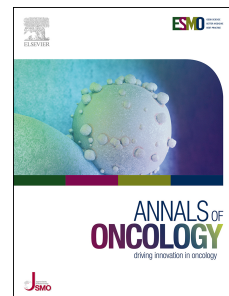
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3 **Seroconversion in patients with cancer and oncology healthcare workers infected by SARS-**
4 **CoV-2**

5

6 **Running head:** Seroconversion in patients with cancer and COVID-19

7

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33

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40 **Highlights**

- 41 • Patients with cancer have high risk for severe complications and poor outcome to
42 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-related disease
43 (coronavirus disease 2019 [COVID-19]).
- 44 • No difference in terms of anti-SARS-CoV-2 immunoglobulin-G (IgG) positivity rates by
45 rapid qualitative membrane-based immunoassay was observed between cancer patients
46 and health workers
- 47 • Median time from SARS-CoV-2 diagnosis to IgG detection was comparable between
48 cancer patients and health workers
- 49 • Our data showed that SARS-CoV-2-specific IgG antibody detection is not different
50 between cancer patients and healthy subjects

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64 Abstract**65 Background**

66 Patients with cancer have high risk for severe complications and poor outcome to severe acute
67 respiratory syndrome coronavirus 2 (SARS-CoV-2)-related disease (coronavirus disease 2019
68 [COVID-19]). Almost all subjects with COVID-19 develop anti-SARS-CoV-2 immunoglobulin-G
69 (IgG) within three weeks after infection. No data are available on the seroconversion rates of
70 cancer patients and COVID-19.

71 Material and methods

72 We conducted a multicenter, observational, prospective study that enrolled: 1) patients and
73 oncology health professionals with SARS-CoV-2 infection confirmed by real time polymerase
74 chain reaction (RT-PCR) assays on nasal/pharyngeal swab specimens; 2) patients and oncology
75 health professionals with clinical or radiological suspicious of infection by SARS-CoV-2; and 3)
76 patients with cancer who are considered at high risk for infection and eligible for active therapy
77 and/or major surgery. All enrolled subjects were tested with the 2019-nCoV IgG/IgM Rapid Test
78 Cassette, which is a qualitative membrane-based immunoassay for the detection of IgG and
79 IgM antibodies to SARS-CoV-2. The aim of the study was to evaluate anti-SARS-CoV-2
80 seroconversion rate in patients with cancer and oncology healthcare professionals with
81 confirmed or clinically suspected COVID-19.

82 Results

83 From March 30 to May 11, 2020, 166 subjects were enrolled in the study. Among them, cancer
84 patients and health workers were 61 (36.7%) and 105 (63.3%), respectively. Overall, 86 subjects
85 (51.8%) had confirmed SARS-CoV-2 diagnosis by RT-PCR testing on nasopharyngeal swab
86 specimen, while 60 (36.2%) had a clinical suspicious of COVID-19. Median time between
87 symptom onset (for cases not confirmed by RT-PCR) or RT-PCR confirmation to serum antibody
88 test was 17 days (interquartile range, 26). In the population with confirmed RT-PCR, 83.8% was
89 IgG positive. No difference in IgG positivity was observed between cancer patients and health
90 workers (87.9% vs 80.5%; $P = 0.39$).

91 **Conclusions**

92 Our data indicate that SARS-CoV-2-specific IgG antibody detection do not differ between cancer
93 patients and healthy subjects

94

95 **Keywords:** cancer; healthcare workers; COVID-19; SARS-CoV-2; coronavirus; antibody response;
96 seroconversion

Journal Pre-proof

97 Introduction

98 Since its first reported case in late December of 2019, the outbreak of the severe acute
99 respiratory syndrome coronavirus 2 (SARS-CoV-2)-related disease (coronavirus disease 2019
100 [COVID-19]) has rapidly spread around the world. As of July 29, 2020, more than 16 million
101 confirmed cases and 650,000 deaths related to COVID-19 have been reported worldwide [1].
102 Since the beginning of the epidemic, subjects with chronic diseases such as cancer have been
103 shown to have an increased risk of severe complications and poor outcomes with COVID-19 [2-
104 5]. Patients with cancer are more susceptible to infection than general population because of
105 their systemic immunosuppressive state [6]. Accordingly, some studies reported that patients
106 with cancer have a higher risk of severe outcomes related to COVID-19, including death,
107 intensive care unit (ICU) admission, development of severe/critical symptoms, and utilization of
108 invasive mechanical ventilation, compared with patients without cancer [7, 8]. Several factors,
109 including increased age, male sex, active or former smoking, poor performance status and
110 active cancer, have been associated with high thirty-day mortality rate in patients with cancer
111 and COVID-19 [9]. Moreover, patients with cancer who underwent chemotherapy or surgery
112 seem to be at high risk of clinical severe events [7, 8, 10], although other studies did not
113 confirm this observation [9, 11] On the other hand, patients with cancer and COVID-19 can also
114 experience a spectrum of asymptomatic or *pauci*-symptomatic infections with subclinical
115 courses [12], being managed at home and referred to the telemedicine systems or primary
116 healthcare network [13].

117 Reverse transcription-polymerase chain reaction (RT-PCR) has demonstrated to be a sensitive
118 methodology and can effectively confirm SARS-CoV-2 infection [14]. Studies on severe acute
119 respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) showed that virus-
120 specific antibodies were detectable in 80-100% of patients at 2 weeks after symptom onset [15-
121 17]. Similarly, almost all patients with COVID-19 are tested as positive for anti- SARS-CoV-2
122 immunoglobulin-G (IgG) within 19 days after symptom development [18]. Furthermore,
123 combining viral RNA by RT-PCR and antibody detections significantly improves the sensitivity of
124 pathogenic diagnosis for COVID-19 [19]. However, very limited information on the antibody
125 responses against SARS-CoV-2 in patients with cancer is currently available, with two

126 retrospective analyses on small populations of cancer patients that reported lower detection
127 rates of SARS-CoV-2 antibodies [20, 21].

128 This article reports the first analysis of a prospective observational study aimed to evaluate the
129 antibody response in cancer patients and oncology healthcare workers presenting with
130 confirmed or clinically suspected COVID-19.

131

132 **Material and methods**

133 ***Study design***

134 This study was a multicenter, observational, prospective study conducted at five Italian
135 Institutions. At time of this interim analysis, a total of 166 subjects were enrolled in this study
136 from one general hospital and one comprehensive cancer center in Lombardy Region, which
137 was the epicenter of the COVID-19 epidemic in Italy [22, 23]. Study population included three
138 different categories: 1) patients or health professionals already confirmed to be positive for
139 SARS-CoV-2 by RT-PCR assays on nasal/pharyngeal swab specimens; 2) patients or health
140 professionals who are suspected of being infected with SARS-CoV-2, defined as history of
141 contact with confirmed cases before the onset of illness or subjects with at least one clinical
142 manifestation or imaging characteristics of COVID-19 in the last week before accrual in the trial;
143 3) patients with cancer who are considered at high risk for infection and eligible for active
144 therapy and/or major surgery. Subjects diagnosed with bacterial or viral pneumonia in previous
145 three months were excluded from the study. **Figure S1** graphically represents a flow chart with
146 the enrolled subjects.

147 Institutional review board and Ethics committee approval was obtained from all participating
148 Institutions. The study was conducted in accordance with the Declaration of Helsinki. All
149 patients provided written informed consent before any study-related procedure.

150

151 ***Detection of SARS-CoV-2 RNA by RT-PCR***

152 Presence of SARS-CoV-2 on nasopharyngeal swab specimens was determined by means real-
153 time RT-PCR. GeneFinder™ COVID-19 Plus RealAmp Kit (Elitech, Milan, Italy) or Allplex™ 2019
154 n-CoV Assay (Seegene Inc, Seoul, South Korea) were used to detect SARS-CoV-2 by amplification
155 of RdRp gene, E gene and N gene according to the World Health Organization (WHO)
156 recommendations and as previously described [24].

157 Overall, 836 specimens obtained from nasopharyngeal swab were tested by RT-PCR.

158

159 ***Detection of IgG and IgM against SARS-CoV-2***

160 To evaluate the presence of IgG and IgM against SARS-CoV-2, all enrolled subjects were tested
161 with the *2019-nCoV IgG/IgM Rapid Test Cassette*® (PRIMA Lab SA, Balerna, Switzerland), which
162 is a qualitative membrane based immunoassay for the detection of IgG and IgM antibodies to
163 SARS-CoV-2 in whole blood, serum or plasma specimen. For this purpose, capillary blood was
164 obtained from each subject by fingerstick. After a droplet was formed, capillary blood was
165 captured in a capillary tube until filled to approximately 20 µL. The whole blood was then
166 dispensed to the specimen well of the test cassette. Lastly, two drops of diluent were added to
167 the specimen well of the test cassette.

168 The *2019-nCoV IgG/IgM Rapid Test Cassette*® consists of two components, an IgG component
169 and an IgM component. In the IgG component, anti-human IgG is coated in IgG test line region.
170 During testing, the specimen reacts with 2019-nCoV antigen-coated particles in the test
171 cassette. The mixture then migrates upward on the membrane chromatographically by capillary
172 action and reacts with the anti-human IgG in IgG test line region, if the specimen contains IgG
173 antibodies to 2019-nCoV. Anti-human IgM is coated in IgM test line region and if specimen
174 contains IgM antibodies to 2019-nCoV, the conjugate-specimen complex reacts with anti-
175 human IgM. If the specimen contains 2019-nCoV IgG antibodies, a colored line appears in IgG
176 test line region as a result of this. Similarly, a colored line appears in IgM test line region, if the
177 specimen contains 2019-nCoV IgM antibodies. If the specimen does not contain 2019-nCoV
178 antibodies, no colored line appears in either of the test line regions, indicating a negative result.

179 To serve as a procedural control, a colored line always appears in the control line region,
180 indicating that the proper volume of specimen has been added and membrane wicking has
181 occurred. **Figure S2** displays three possible results and interpretation of the rapid test. Overall,
182 166 (one for each enrolled subject) serological rapid tests were performed.

183

184 ***Aim of the study***

185 Primary endpoint of the study was to evaluate anti-SARS-CoV-2 seroconversion rates in cancer
186 patients and cancer health professionals with confirmed or clinically suspected COVID-19.

187

188 ***Statistical analyses***

189 Descriptive statistics were used to analyze and report patients' characteristics. Clinical and
190 biological variables were stratified into categories whenever reasonable, to preserve statistical
191 power and feasibility of data collection. Continuous variables are expressed as the median
192 (interquartile range, IQR) and were compared with the Mann-Whitney U-test. Categorical
193 variables are expressed as numbers and proportions (%) and were compared by Fisher's exact
194 test or Chi-square test, as appropriate. All tests were performed 2-sided at a significance level
195 of $\alpha=0.05$. Statistical analyses were performed using SAS (version 9.4) and R Studio (version
196 1.1.463).

197

198 **Results**

199 From March 30, 2020 to May 11, 2020, 166 subjects were enrolled in the study. Among them,
200 cancer patients and health workers were 61 (36.7%) and 105 (63.3%), respectively. Median age
201 was 46 years (IQR, 21) and 118 (71.1%) were females. Health workers were younger than
202 patients (median age 41 vs 62 years; $P < 0.001$). Patients with cancer were more frequently
203 diagnosed with hypertension (26.2% vs 2.9%; $P < 0.001$) and type 2 diabetes (8.2% vs 1.0%; $P =$
204 0.01) as compared to healthcare workers. Conversely, healthcare workers were more

205 frequently carriers of autoimmune diseases (12.4% vs 3.3%; $P = 0.04$), mainly chronic
206 autoimmune thyroiditis and rheumatoid arthritis (data not showed). Patients' characteristics
207 are reported in **Table 1**.

208 Among 61 cancer patients, breast carcinoma was the most frequent diagnosed tumor (55.7%),
209 followed by lung cancer (13.1%). Thirty-three (54.1%) had metastatic disease. Forty-one (67.2%)
210 patients were receiving active antitumoral therapies, that included systemic chemotherapy
211 (14.8%), immunotherapy (8.2%), targetted therapy (9.8%), and hormonal therapy +/- targetted
212 therapy (6.6% and 29.5%, respectively). Main characteristics of enrolled patients with cancer
213 are described in **Table S1**.

214 Overall, 86 subjects (51.8%) had confirmed SARS-CoV-2 diagnosis by prior RT-PCR testing on
215 nasopharyngeal swab specimen, while 60 (36.2%) and 20 (12.0%) were clinically suspected or at
216 high risk for SARS-CoV-2 infection, respectively. The majority (79.2%) were diagnosed with mild
217 COVID-19 condition, according to the *Italian Society for Anesthesia, Analgesia, Resuscitation*
218 *and Intensive Care* (SIAARTI) clinical classification, while 11.7% and 9.1% as moderate and
219 severe, respectively.

220 Median time between symptom onset (for cases not confirmed by RT-PCR) or RT-PCR
221 confirmation to serum antibody test was 17 days (IQR, 26), while median time to symptom
222 resolution or viral RT-PCR negativization was 22 days (IQR, 33). Of note, 9 subjects (5.4%) still
223 had RNA viral detection by RT-PCR on swab specimen at time of this analysis.

224

225 ***Detection of IgG against SARS-CoV-2 in subjects with positive RT-PCR***

226 In the overall population, 69 (41.6%) and 3 (1.8%) participants were IgG and IgM positive,
227 respectively. Considering the population with confirmation by RT-PCR, 62 (83.8%) was IgG
228 positive (**Table 2**). No difference in terms of IgG positivity was observed between cancer
229 patients and health workers (87.9% vs 80.5%; $P = 0.39$) (**Figure 1**). Furthermore, no differences
230 were observed in time from SARS-CoV-2 diagnosis to IgG detection between cancer patients
231 and health workers (23.0 vs 28.0 days; $P = 0.21$) (**Table 3; Figures 2 and 3**). Age, gender,

232 comorbidities, and symptom intensity did not significantly influence rate and time of IgG
233 antibody response.

234

235 **Discussion**

236 According to the European Commission recommendations [25], timely and accurate SARS-CoV-
237 2 laboratory testing is an essential part of the management of COVID-19 for slowing down the
238 pandemic, supporting decisions on infection control strategies and patient management at
239 healthcare facilities, and detecting asymptomatic cases that could spread the virus further if not
240 isolated.

241 Rapid tests are non-automated procedures and have been designed to give a fast result. For
242 COVID-19, rapid tests may take around 10-15 minutes until giving a result compared with about
243 four hours for molecular tests [26]. These rapid tests are relatively simple to perform and
244 interpret and therefore require limited test operator training. They may be intended either for
245 use in hospital for particular situations or in other social needs, allowing rapid screening of
246 symptomatic and asymptomatic SARS-CoV-2 carriers.

247 Our findings suggest that patients with cancer infected with SARS-CoV-2 tend to have an
248 antibody response comparable to healthy subjects, who in our population were represented by
249 healthcare workers. Understanding the duration of potential infectiousness and the time to IgG
250 antibody response are critical to the containment of SARS-CoV-2 spread, especially in cancer
251 patients and healthcare workers who are in constant exposure to high-risk populations.
252 Moreover, monitoring previously infected subjects is essential to optimize the adequate
253 individual protection diapositives, the clinical management and the administration of
254 oncological treatments.

255 Patients with cancer are at higher risk of developing infections for several factors that include
256 advanced age, underlying immunosuppressive status, and treatment-related factors such as
257 chemotherapy, radiation, and surgical procedures [27]. Accordingly, several works reported
258 that patients with cancer have a higher risk of severe outcomes related to COVID-19 [7-11].

259 In contrast to prior literature [20, 21], our experience showed that more than 85% of the cancer
260 patients who had laboratory documented SARS-CoV-2 infection or high clinical suspicious
261 developed IgG antibodies using our rapid assay. Notably, no differences in terms of antibody
262 formation and time to seroconversion were observed in cancer patients as compared to
263 healthcare workers. Given that cytotoxic agents are able to dampen immune response and
264 interfere with antibody formation [28], it could be expected that patients on chemotherapy
265 have lower rates of antibody positivity [20]. Of note, more than 60% of our patients were
266 receiving active treatments, but only a minority (about 10%) chemotherapy. Accordingly, such
267 association needs to be confirmed in larger cohorts of patients with cancer and COVID-19.

268 Additionally, our findings suggest that IgG antibodies develop over a median period of 17 days
269 from symptom onset or RT-PCR confirmation. This suggests that the ideal time frame for
270 antibody testing is at least two weeks after symptom onset and no more than three/four weeks
271 after symptom resolution or RT-PCR negativization. As reported by Long et al. [18], antibody
272 testing should be performed as early as possible, because about 12% of the patients had
273 already plateaued in IgG titer within seven days of symptom onset. For patients who were not
274 sampled during the ideal window or are tested at later stages, repeated serological tests would
275 be needed to confirm an antibody response against SARS-CoV-2 infection. Comparable data
276 were recently reported in a preprint paper summarizing the results of a study conducted in the
277 New York region (United States) [29]. Moreover, considering that many infected patients
278 remain asymptomatic and fully capable of transmitting SARS-CoV-2 [30, 31], combining
279 antibody testing and RT-PCR on swab specimen can potentially increase COVID-19 diagnosis.

280 Although scant information on the immunity conferred by IgG and its duration, previous
281 experiences in other viral infections, such as SARS and MERS, suggest that IgG may confer some
282 level of immunity [32, 33], while it seems to wane over the time. Similar data have been
283 reported for other coronaviruses where immunity can confer limited protection [34]. In order to
284 study the duration of IgG antibody response to SARS-CoV-2, we planned to prospectively follow
285 our patient population and retest for IgG by both quantitative and qualitative assays after three
286 and six months in order to measure time and level of immunization. Moreover, blood samples
287 from each enrolled subject will be analyzed to evaluate also quantitative IgG and IgM levels in

288 the peripheral blood. At time of the present analysis, data on antibody titer were available only
289 for 16.9% of the overall population (data not shown).

290 Among subjects who had not a confirmed infection by RT-PCR, but were considered as clinical
291 suspected or high risk, including those with symptoms consistent with COVID-19, highly
292 suggestive radiological imaging or close contact with patients with confirmed SARS-CoV-2
293 infection, we found that only 8.8% of this population had IgG antibodies. This finding suggests
294 that a majority of participants suspected for COVID-19 actually were not infected with SARS-
295 CoV-2. In addition, recent evidences suggested weaker immune responses and a more rapid
296 reduction in the IgG titer for asymptomatic individuals infected by SARS-CoV-2 as compared to
297 symptomatic subjects [35]. On the other hand, the low rates of IgG positivity in subjects
298 without a confirmed diagnosis of SARS-CoV-2 infection by RT-PCR may be related to a false
299 negative rate of our assay or insufficient time for participants to mount an IgG antibody
300 response detectable by means rapid test. This remarks the importance of harmonize and
301 validate proper methodologies for SARS-CoV-2 detection to improve diagnosis and reduce false
302 negative rates.

303 Notably, nine subjects (5.4%) remained RT-PCR positive despite full resolution of symptoms and
304 IgG seroconversion. This had relevant implications regarding the real duration of viral
305 transmission. Although other viral genomes can be detected even months after resolution of
306 clinical infection [36], additional research on SARS-CoV-2 is need to determine if
307 nasopharyngeal RT-PCR positivity is related to transmission and the duration of the viral
308 shedding [37].

309 We are aware that our study presents some limitations. About 90% of participants had mild
310 disease, and thus these data may not reflect antibody response in moderate or severe COVID-
311 19. Furthermore, we did not collect rigorous data regarding symptom severity which could
312 potentially be related to the timeline and strength of IgG antibody response to SARS-CoV-2. As
313 aforementioned, further studies are needed to understand the magnitude and duration of the
314 IgG response in patients recovered from SARS-CoV-2. In addition, the antibody titer that is
315 necessary to protect individuals from reinfection is currently unknown. Lastly, the clinical

316 significance of prolonged positive SARS-CoV-2 nasopharyngeal PCR in the absence of clinical
317 evidence requires additional clarification.

318 Of note, only 19% of healthcare workers in our study population reported having received
319 seasonal flu vaccine. Although WHO and national agencies identify health workers as a priority
320 target group and recommend for vaccination, influenza vaccination coverage rates of
321 healthcare workers are significantly variable in Europe, ranging from 15.6% to 63.2% [38]. In
322 Italy, the coverage rate is very low (less than 20%), as showed in a multicenter cross-sectional
323 study conducted in ten Italian cities [39]. These observations have relevant implications related
324 to the current COVID-19 pandemic, especially considering the overlapping between seasonal
325 flu- and COVID-19-related symptoms. In order to plan organization and management of future
326 COVID-19 waves, it might be to guarantee influenza vaccination coverage for all healthcare
327 workers. **Conclusions**

328 Our data indicate that SARS-CoV-2-specific IgG antibody detection is not different between
329 cancer patients and healthy subjects. As a result, rapid test for antibody detection can be a
330 complement to RNA RT-PCR testing for the diagnosis of COVID-19, especially in those situations
331 where the knowledge of the COVID-19 status is rapidly mandatory for specific clinical decisions.
332 In vulnerable population such as cancer patients, confirming suspected COVID-19 cases as early
333 as possible with the help of serological testing could reduce exposure risk and help optimizing
334 diagnostic and therapeutic algorithms. The key for success in COVID-19 and cancer is to
335 implement diagnostic and therapeutic methodologies, maybe with a high sensitivity/sensibility
336 and rapidity of execution/resulting that allow to ensure a continuum of the healthcare during
337 pandemic.

338

339

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352 **Author's contribution:** Study concept and design: GC, DG, AM. Acquisition, analysis, and
353 interpretation of data: AM, SG, PZ, DG, GC. Drafting of the manuscript: AM and GC. Statistical
354 analysis: SG and AM. Administrative, technical, or material support: All authors. Study
355 supervision: GC. All the authors read and approved the final version of the manuscript.

356 **Ethics approval and consent to participate:** Institutional review board and Ethics committee
357 approval was obtained from all participating Institutions. The study was conducted in
358 accordance with the Declaration of Helsinki. All the patients provided written informed consent
359 before any study-related procedures.

360 **Availability of data and material:** All data generated or analyzed during this study are included
361 in the published article. Additional supporting data are available from the corresponding author
362 on reasonable request. All requests for raw and analyzed data and materials will be reviewed
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368 **References**

- 369 1. World Health Organization. Coronavirus disease 2019 (COVID-19) Situation Report - 191.
370 Available at: [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200729-](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200729-covid-19-sitrep-191.pdf?sfvrsn=2c327e9e_2)
371 [covid-19-sitrep-191.pdf?sfvrsn=2c327e9e_2](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200729-covid-19-sitrep-191.pdf?sfvrsn=2c327e9e_2). Accessed on: 29 July 2020.
- 372 2. Guan WJ, Ni ZY, Hu Y et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J*
373 *Med* 2020.
- 374 3. Chen N, Zhou M, Dong X et al. Epidemiological and clinical characteristics of 99 cases of 2019
375 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; 395: 507-513.
- 376 4. Wu C, Chen X, Cai Y et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and
377 Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med* 2020.
- 378 5. Mehta V, Goel S, Kabarriti R et al. Case Fatality Rate of Cancer Patients with COVID-19 in a New
379 York Hospital System. *Cancer Discov* 2020.
- 380 6. Kamboj M, Sepkowitz KA. Nosocomial infections in patients with cancer. *Lancet Oncol* 2009; 10:
381 589-597.
- 382 7. Liang W, Guan W, Chen R et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in
383 China. *Lancet Oncol* 2020; 21: 335-337.
- 384 8. Dai M, Liu D, Liu M et al. Patients with cancer appear more vulnerable to SARS-COV-2: a multi-
385 center study during the COVID-19 outbreak. *Cancer Discov* 2020.
- 386 9. Kuderer NM, Choueiri TK, Shah DP et al. Clinical impact of COVID-19 on patients with cancer
387 (CCC19): a cohort study. *Lancet* 2020; 395: 1907-1918.
- 388 10. Zhang L, Zhu F, Xie L et al. Clinical characteristics of COVID-19-infected cancer patients: a
389 retrospective case study in three hospitals within Wuhan, China. *Ann Oncol* 2020.
- 390 11. Pinato DJ, Zambelli A, Aguilar-Company J et al. Clinical portrait of the SARS-CoV-2 epidemic in
391 European cancer patients. *Cancer Discovery* 2020; CD-20-0773.
- 392 12. Li R, Pei S, Chen B et al. Substantial undocumented infection facilitates the rapid dissemination
393 of novel coronavirus (SARS-CoV-2). *Science* 2020; 368: 489-493.
- 394 13. Trapani D, Marra A, Curigliano G. The experience on coronavirus disease 2019 and cancer from
395 an oncology hub institution in Milan, Lombardy Region. *Eur J Cancer* 2020; 132: 199-206.
- 396 14. Zou L, Ruan F, Huang M et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected
397 Patients. *N Engl J Med* 2020; 382: 1177-1179.
- 398 15. Li G, Chen X, Xu A. Profile of specific antibodies to the SARS-associated coronavirus. *N Engl J*
399 *Med* 2003; 349: 508-509.
- 400 16. Drosten C, Meyer B, Muller MA et al. Transmission of MERS-coronavirus in household contacts.
401 *N Engl J Med* 2014; 371: 828-835.
- 402 17. Meyer B, Drosten C, Muller MA. Serological assays for emerging coronaviruses: challenges and
403 pitfalls. *Virus Res* 2014; 194: 175-183.
- 404 18. Long QX, Liu BZ, Deng HJ et al. Antibody responses to SARS-CoV-2 in patients with COVID-19. *Nat*
405 *Med* 2020.
- 406 19. Zhao J, Yuan Q, Wang H et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus
407 disease 2019. *Clin Infect Dis* 2020.
- 408 20. Solodky ML, Galvez C, Russias B et al. Lower detection rates of SARS-COV2 antibodies in cancer
409 patients vs healthcare workers after symptomatic COVID-19. *Ann Oncol* 2020.
- 410 21. Liu T, Zeng G, Tao H et al. Low prevalence of IgG antibodies to SARS-CoV-2 in cancer patients
411 with COVID-19. *Int J Cancer* 2020.
- 412 22. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? *Lancet* 2020.
- 413 23. Spina S, Marrazzo F, Migliari M et al. The response of Milan's Emergency Medical System to the
414 COVID-19 outbreak in Italy. *Lancet* 2020; 395: e49-e50.

- 415 24. Corman VM, Landt O, Kaiser M et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-
416 time RT-PCR. *Euro Surveill* 2020; 25.
- 417 25. European Commission. COVID-19 - EU recommendations for testing strategies. Available at:
418 [https://ec.europa.eu/info/sites/info/files/covid19_-](https://ec.europa.eu/info/sites/info/files/covid19_-_eu_recommendations_on_testing_strategies_v2.pdf)
419 [_eu_recommendations_on_testing_strategies_v2.pdf](https://ec.europa.eu/info/sites/info/files/covid19_-_eu_recommendations_on_testing_strategies_v2.pdf). Accessed on: 14 May 2020.
- 420 26. Li Z, Yi Y, Luo X et al. Development and clinical application of a rapid IgM-IgG combined antibody
421 test for SARS-CoV-2 infection diagnosis. *J Med Virol* 2020.
- 422 27. Rolston KV. Infections in Cancer Patients with Solid Tumors: A Review. *Infect Dis Ther* 2017; 6:
423 69-83.
- 424 28. Bracci L, Schiavoni G, Sistigu A, Belardelli F. Immune-based mechanisms of cytotoxic
425 chemotherapy: implications for the design of novel and rationale-based combined treatments against
426 cancer. *Cell Death Differ* 2014; 21: 15-25.
- 427 29. Wajnberg A, Mansour M, Leven E et al. Humoral immune response and prolonged PCR positivity
428 in a cohort of 1343 SARS-CoV 2 patients in the New York City region. *medRxiv* 2020;
429 2020.2004.2030.20085613.
- 430 30. Bai Y, Yao L, Wei T et al. Presumed Asymptomatic Carrier Transmission of COVID-19. *JAMA* 2020.
- 431 31. Rothe C, Schunk M, Sothmann P et al. Transmission of 2019-nCoV Infection from an
432 Asymptomatic Contact in Germany. *N Engl J Med* 2020; 382: 970-971.
- 433 32. Cao WC, Liu W, Zhang PH et al. Disappearance of antibodies to SARS-associated coronavirus
434 after recovery. *N Engl J Med* 2007; 357: 1162-1163.
- 435 33. Al-Abdely HM, Midgley CM, Alkhamis AM et al. Middle East Respiratory Syndrome Coronavirus
436 Infection Dynamics and Antibody Responses among Clinically Diverse Patients, Saudi Arabia. *Emerg*
437 *Infect Dis* 2019; 25: 753-766.
- 438 34. Huang AT, Garcia-Carreras B, Hitchings MDT et al. A systematic review of antibody mediated
439 immunity to coronaviruses: antibody kinetics, correlates of protection, and association of antibody
440 responses with severity of disease. *medRxiv* 2020; 2020.2004.2014.20065771.
- 441 35. Long QX, Tang XJ, Shi QL et al. Clinical and immunological assessment of asymptomatic SARS-
442 CoV-2 infections. *Nat Med* 2020.
- 443 36. Lin WH, Kouyos RD, Adams RJ et al. Prolonged persistence of measles virus RNA is characteristic
444 of primary infection dynamics. *Proc Natl Acad Sci U S A* 2012; 109: 14989-14994.
- 445 37. He X, Lau EHY, Wu P et al. Temporal dynamics in viral shedding and transmissibility of COVID-19.
446 *Nat Med* 2020.
- 447 38. European Centre for Disease Prevention and Control (ECDC). Seasonal influenza vaccination and
448 antiviral use in EU/EEA Member States: Overview of vaccine recommendations for 2017-2018 and
449 vaccination coverage rates for 2015-2016 and 2016-2017 influenza seasons. Stockholm: ECDC; Nov
450 2018. Available at: [https://ecdc.europa.eu/sites/portal/files/documents/seasonal-influenza-antiviral-](https://ecdc.europa.eu/sites/portal/files/documents/seasonal-influenza-antiviral-use-2018.pdf)
451 [use-2018.pdf](https://ecdc.europa.eu/sites/portal/files/documents/seasonal-influenza-antiviral-use-2018.pdf). Accessed on: 29 July 2020.
- 452 39. Genovese C, Picerno IAM, Trimarchi G et al. Vaccination coverage in healthcare workers: a
453 multicenter cross-sectional study in Italy. *J Prev Med Hyg* 2019; 60: E12-E17.

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456 **Table 1.** Patients' characteristics. Abbreviations: ACE, angiotensin-converting enzyme; ARB,
 457 angiotensin receptor blockers; ICU, intensive care unit; IgG, immunoglobulin G; IgM,
 458 immunoglobulin M; IQR, interquartile range; NA, not applicable; RT-PCR, reverse transcriptase-
 459 polymerase chain reaction.

	Health workers (N=105)	Cancer patients (N=61)	Total (N=166)	<i>P</i> value
Age				<0.001
Median (IQR)	41 (14)	62 (21)	46 (21)	
Gender				0.629
Female	76 (72.4%)	42 (68.9%)	118 (71.1%)	
Male	29 (27.6%)	19 (31.1%)	48 (28.9%)	
Seasonal flu vaccine				0.548
No	85 (81.0%)	47 (77.0%)	132 (79.5%)	
Yes	20 (19.0%)	14 (23.0%)	34 (20.5%)	
Comorbidities				
Cardiovascular	3 (2.9%)	2 (3.3%)	5 (3.0%)	0.878
Pulmonary	0 (0.0%)	2 (3.3%)	2 (1.2%)	0.062
Asthma	7 (6.7%)	2 (3.3%)	9 (5.4%)	0.353
Diabetes	1 (1.0%)	5 (8.2%)	6 (3.6%)	0.016
Autoimmunity	13 (12.4%)	2 (3.3%)	15 (9.0%)	0.049
Hypertension	3 (2.9%)	16 (26.2%)	19 (11.4%)	<0.001
Concomitant drugs				
ARB	1 (1.0%)	3 (4.9%)	4 (2.4%)	0.108
ACE inhibitor	2 (1.9%)	4 (6.6%)	6 (3.6%)	0.122
Inclusion criteria				<0.001
Confirmed	56 (53.3%)	30 (49.2%)	86 (51.8%)	
High Risk	0 (0.0%)	20 (32.8%)	20 (12.0%)	
Suspected	49 (46.7%)	11 (18.0%)	60 (36.2%)	
Contact with infected subject				<0.001
NA	39	27	66	
No	16 (15.2%)	22 (36.1%)	38 (22.9%)	
Yes	50 (47.6%)	12 (19.7%)	62 (37.3%)	
Presentation				0.226

NA	60	29	89	
Mild	38 (84.4%)	23 (71.9%)	61 (79.2%)	
Moderate	5 (11.1%)	4 (12.5%)	9 (11.7%)	
Severe	2 (4.4%)	5 (15.6%)	7 (9.1%)	
Setting of care				0.084
NA	59	29	88	
Home	45 (97.8%)	27 (84.4%)	72 (92.3%)	
Hospital	1 (2.2%)	4 (12.5%)	5 (6.4%)	
ICU	0 (0.0%)	1 (3.1%)	1 (1.3%)	
Ventilation				0.273
No	103 (98.1%)	58 (95.1%)	161 (97.0%)	
Yes	2 (1.9%)	3 (4.9%)	5 (3.0%)	
Complications				<0.001
None	101 (96.2%)	47 (77.0%)	148 (89.2%)	
Pneumonitis	4 (3.8%)	14 (23.0%)	18 (10.8%)	
Outcome				0.229
Ongoing	4 (3.8%)	5 (8.2%)	9 (5.4%)	
Recovered	101 (96.2%)	56 (91.8%)	157 (94.6%)	
IgG				0.030
Negative	68 (64.8%)	29 (47.5%)	97 (58.4%)	
Positive	37 (35.2%)	32 (52.5%)	69 (41.6%)	
IgM				0.902
Negative	103 (98.1%)	60 (98.4%)	163 (98.2%)	
Positive	2 (1.9%)	1 (1.6%)	3 (1.8%)	
RT-PCR testing				<0.001
No	21 (20.0%)	0 (0.0%)	21 (12.7%)	
Yes	84 (80.0%)	61 (100.0%)	145 (87.3%)	
RT-PCR result				0.529
NA	21	0	21	
Negative	43 (51.2%)	28 (45.9%)	71 (49.0%)	
Positive	41 (48.8%)	33 (54.1%)	74 (51.0%)	

460

461

462

463 **Table 2.** IgM and IgG seroconversion in overall population, cancer patient and health workers.
 464 Abbreviations: IgG, immunoglobulin G; IgM, immunoglobulin M; RT-PCR, reverse transcriptase-
 465 polymerase chain reaction.

		RT-PCR-negative (N=71)	RT-PCR-positive (N=74)	Total (N=145)	<i>P</i> value
Overall	IgG				<0.001
	Negative	65 (91.5%)	12 (16.2%)	77 (53.1%)	
	Positive	6 (8.5%)	62 (83.8%)	68 (46.9%)	
	IgM				0.535
	Negative	69 (97.2%)	73 (98.6%)	142 (97.9%)	
	Positive	2 (2.8%)	1 (1.4%)	3 (2.1%)	
Cancer patients	IgG				<0.001
	Negative	25 (89%)	4 (12%)	29 (20%)	
	Positive	3 (11%)	29 (88%)	32 (22%)	
Health workers	IgG				<0.001
	Negative	40 (93%)	8 (20%)	48 (33%)	
	Positive	3 (7%)	33 (80%)	36 (25%)	

466

467

468

469 **Table 3. Median time to IgG positivization.** Abbreviations: IQR, interquartile range; Q1, 1st
 470 quartile; Q3, 3rd quartile.

		Median (IQR)	Q1	Q3	<i>P</i> value
Category	Health workers	23.0 (13.0)	17	29	0.208
	Patients	28.0 (19.2)	16	35	
Gender	Female	25.0 (16.5)	16	34	0.761
	Male	27.0 (17.7)	16	34	

471

472

473 **Figure legends**

474

475 **Figure 1. Comparison between IgG positivity rate between healthcare workers (red) and**
476 **patients with cancer (blue) according to the result of reverse transcriptase-polymerase chain**
477 **reaction (RT-PCR) test for SARS-CoV-2. *P* value refers to the Fisher's exact test. Abbreviations:**
478 **HCWs, healthcare workers; RT-PCR, reverse transcriptase-polymerase chain reaction**

479

480 **Figure 2. Comparison between time to IgG seroconversion and subject category (health**
481 **workers vs patients, panel a) and gender (female vs male, panel b). On each box, the central**
482 **mark is the median, the edges of the box are the 25th and 75th percentiles, the whiskers extend**
483 **to the most extreme data points not considered outliers, and outliers are plotted individually. *P***
484 **value refers to the Mann-Whitney U-test.**

485

486 **Figure 3. Cumulative incidence of seroconversion of IgG antibodies against SARS-CoV-2**
487 **among COVID-19 healthcare workers (red line) and cancer patients (blue line).**

488 **Figure S1 graphically represents a flow chart with the enrolled subjects.**

489 **Figure S2 displays three possible results and interpretation of the rapid test.**

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