



Risk factors for Coronavirus Disease 2019 (COVID-19) severity and mortality among solid cancer patients and impact of the disease on anticancer treatment: A French nationwide cohort study (GCO-002 CACOVID-19).

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Author Contributions Section

AL, AT, IRC, KLM, JT, OB, ACHB, DD, GZ and TA conceived and designed the study. AL and KLM designed the statistical analysis plan, analysed the data and developed the figures and tables. All authors except KLM and XP, coordinated data contributions at their respective sites and provided patients' data.

All authors contributed intellectual content during the drafting and revision of the work and approved the final version.

Risk factors for COVID-19 severity and mortality among solid cancer patients and its impact on anticancer treatment: a nationwide cohort study (GCO-002 CACOV1D-19)

Astrid Lièvre¹, Anthony Turpin², Isabelle Ray-Coquard³, Karine Le Malicot⁴, Juliette Thariat⁵, Guido Ahle⁶, Cindy Neuzillet⁷, Xavier Paoletti⁷, Olivier Bouché⁸, Kais Aldabbagh⁹, Pierre Michel¹⁰, Didier Debievre¹¹, Anthony Canellas¹², Marie Wislez¹³, Lucie Laurent¹⁴, May Mabro¹⁵, Raphael Colle¹⁶, Anne-Claire Hardy-Bessard¹⁷, Laura Mansi¹⁸, Emeline Colomba¹⁹, Jean Bourhis²⁰, Philippe Gorphe²¹, Yoann Pointreau²², Ahmed Idbaih²³, Renata Ursu²⁴, Anna Luisa Di Stefano²⁵, Gérard Zalcman^{26*}, Thomas Aparicio^{27*} for the GCO-002 CACOV1D-19 collaborators/investigators #

***equally contributed to the work**

1. Department of gastroenterology, University Hospital Pontchaillou, Rennes 1 University, INSERM U1242 "Chemistry Oncogenesis Stress Signaling", Rennes, FFCD, France
- 2 Univ. Lille, CNRS UMR9020, Inserm UMR-S 1277 - Canther - Cancer Heterogeneity, Plasticity and Resistance to Therapies, CHU Lille, Department of Medical Oncology, Lille, GERCOR, France
3. Department of medical oncology, Leon Bérard center, University Claude Bernard Lyon Est, Lyon, ARCAGY-GINECO, France
4. Fédération Francophone de Cancérologie Digestive (FFCD); EPICAD INSERM LNC-UMR 1231, University of Burgundy and Franche Comté, Dijon; France
5. Department of Radiation Oncology, Baclesse Cancer center, Caen, GORTEC/intergroupe ORL, France
6. Department of neurology, Colmar civil hospital, Colmar, ANOCEF-IGCNO, France
7. Department of medical oncology, Curie Institut, Saint-Cloud, France
8. Department of digestive oncology, CHU Reims, Reims, FFCD, France
9. Saint-Côme clinic, Compiègne, FFCD, France
10. Normandie Univ, UNIROUEN, Inserm 1245, IRON group, department of hepatogastroenterology, Rouen University Hospital, Rouen, FFCD, France
11. Pneumology Department, Emile Muller hospital, Mulhouse, IFCT France
12. Pneumology Department, Tenon hospital, Paris, IFCT, France
13. Thoracic oncology unit, Cochin hospital, Paris ; Paris-Descartes University, Paris, IFCT France
14. Department of gastroenterology and pancreatic, Beaujon hospital ; Paris 7 University, Clichy, GERCOR, France
15. Department of oncology, Foch hospital, Suresnes, GERCOR, France
16. Department Medical oncology - Saint-Antoine hospital, Paris, GERCOR, France
17. Armorican Center of Radiotherapy and Radiology, Plérin, ARCAGY-GINECO, France
18. INSERM, EFS BFC, UMR1098, RIGHT, University of Bourgogne Franche-Comté, Interactions Greffon-Hôte-Tumeur/Ingénierie Cellulaire et Génique, ; Department of Medical Oncology, University Hospital of Besancon, ARCAGY-GINECO, Besancon, France

19. Department of medical oncology, Gustave Roussy Cancerology Institute, Villejuif, ARCAGY-GINECO, France
20. Department of radiation oncology, Vaud University Hospital Center (CHUV), Lausanne, GORTEC/intergroupe ORL, Suisse
21. Department of Head and Neck Oncology, Gustave Roussy Cancerology Institute, , Villejuif, GORTEC/intergroupe ORL, France
22. Cancerology Institut -Centre Jean Bernard-Clinique Le Mans, GORTEC/intergroupe ORL, France
23. Sorbonne Université, Inserm, CNRS, UMR S 1127, Institut du Cerveau et de la Moelle épinière, ICM , AP-HP, Hôpitaux Universitaires La Pitié Salpêtrière - Charles Foix, Service de Neurologie 2-Mazarin, Paris, , ANOCEF-IGCNO, France
24. Department of Neurology, Saint Louis hospital, Assistance Publique-Hôpitaux de Paris (AP-HP.Nord); Paris University, ANOCEF-IGCNO, France.
25. Department of Neurology, Foch Hospital, Suresnes, ANOCEF-IGCNO, France
26. Service of thoracic oncology, Université de Paris, INSERM U830: Cancer, Heterogeneity, Instability and Plasticity, Hôpital Bichat-Claude Bernard, AP-HP, Intergroupe Francophone de Cancérologie Thoracique (IFCT), France
27. Department of Gastroenterology, Saint Louis hospital, APHP, Université de Paris, Paris, FFCD, France

Please see the Appendix for a list of the GCO-002 CACOVID-19 collaborators/investigators

Corresponding author: Prof Astrid Lièvre
 Department of gastroenterology, University Hospital Pontchaillou
 2, rue Henri Le Guilloux 35033 Cedex 09, France
 e-mail : astrid.lievre@chu-rennes.fr

Abstract

Background: Cancer patients are thought to have an increased risk of developing severe Coronavirus Disease 2019 (COVID-19) infection and of dying from the disease. In this work, predictive factors for COVID-19 severity and mortality in cancer patients were investigated.

Patients and Methods: In this large nationwide retro-prospective cohort study, we collected data on patients with solid tumours and COVID-19 diagnosed between March 1 and June 11, 2020. The primary endpoint was all-cause mortality and COVID-19 severity, defined as admission to an intensive care unit (ICU) and/or mechanical ventilation and/or death, was one of the secondary endpoints.

Results: From April 4 to June 11, 2020, 1289 patients were analysed. The most frequent cancers were digestive and thoracic. Altogether, 424 (33%) patients had a severe form of COVID-19 and 370 (29%) patients died. In multivariate analysis, independent factors associated with death were male sex (odds ratio 1.73, 95%CI: 1.18-2.52), ECOG PS ≥ 2 (OR 3.23, 95%CI: 2.27-4.61), updated Charlson comorbidity index (OR 1.08, 95%CI: 1.01-1.16) and admission to ICU (OR 3.62, 95%CI 2.14-6.11). The same factors, age along with corticosteroids before COVID-19 diagnosis, and thoracic primary tumour site were independently associated with COVID-19 severity. None of the anticancer treatments administered within the previous 3 months had any effect on mortality or COVID-19 severity, except cytotoxic chemotherapy in the subgroup of patients with detectable SARS-CoV-2 by RT-PCR, which was associated with a slight increase of the risk of death (OR 1.53; 95%CI: 1.00-2.34; $p = 0.05$). A total of 431 (39%) patients had their systemic anticancer treatment interrupted or stopped following diagnosis of COVID-19.

Conclusions: Mortality and COVID-19 severity in cancer patients are high and are associated with general characteristics of patients. We found no deleterious effects of recent anticancer treatments, except for cytotoxic chemotherapy in the RT-PCR-confirmed subgroup of patients. In almost 40% of patients, the systemic anticancer therapy was interrupted or stopped after COVID-19 diagnosis.

Key words: cancer, COVID-19, death, mortality, mechanical ventilation, intensive care unit, chemotherapy, radiotherapy, immunotherapy

1. Introduction

The COronaroVirus Disease 2019 (COVID-19) outbreak, caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2), has spread rapidly around the world. Cancer patients were considered particularly vulnerable to this disease due to immunosuppression linked not only to the underlying malignancy and/or the anticancer treatments, but also to the advanced age, comorbidities and poor performance status or malnutrition frequently found in these patients. This vulnerability was suggested by small retrospective studies [1, 2], and a meta-analysis reported an overall pooled prevalence of cancer of 2% in patients with COVID-19 [3]. Other studies have suggested that patients with cancer have more severe forms of COVID-19 and higher mortality than do patients without cancer [2, 4-6]. However, given the discordant data currently available, the impact of anticancer treatments on COVID-19 severity remains unclear, and there is little in the way of evidence-based data to underpin changes in anticancer treatments made during the peak of the pandemic [1, 6-10]. It is therefore necessary to analyse large cohorts of cancer patients to better understand the course of COVID-19 and the factors likely to have an impact on its severity.

On April 3, 2020 and through the French national network of academic cooperative oncology groups in solid cancers, we set up a large nationwide cohort of solid-tumour cancer patients diagnosed with COVID-19 since March 1. The aims of this cohort study (named GCO-002 CACOVID-19) were to describe clinical and tumour characteristics as well as outcomes in cancer patients with COVID-19, to identify risk factors associated with severity and mortality, in particular concerning active anticancer treatment, and to determine the consequences of the COVID-19 pandemic on the management of cancer care.

2. Material and methods

2.1 Study design

The GCO-002 CACOVID cohort is a French observational nationwide multicentre cohort, set up by the Groupes Coopérateurs en Oncologie (GCO), a French consortium of academic cooperative groups in oncology, including ANOCEF-IGCNO (Association des Neuro-OnCologues d'Expression Française/InterGroupe Coopérateur de Neuro-Oncologie) for central nervous system (CNS) tumours, ARCAGY-GINECO (Association de Recherche sur les Cancers GYNecologiques-Groupes d'Investigateurs Nationaux pour l'étude des Cancers Ovariens et du Sein) for gynaecological and breast cancers, FFCD (Fédération Francophone de Cancérologie Digestive) for digestive cancers, GERCOR (Groupe Coopérateur

Multidisciplinaire en Oncologie), GORTEC (Groupe d'Oncologie Radiothérapie Tête et Cou) with the Intergroupe ORL for head and neck cancers (H&N) and IFCT (Intergroupe Francophone de Cancérologie Thoracique) for thoracic cancers.

The study was approved by the Research Ethics Committee of Caen Normandy University Hospital for all participating centres (Ref: 04/2020/MOR) and obtained the authorization of the National Commission for Data Protection and Liberties (Ref CNIL: MLD/MFI/AR204586). It was registered on ClinicalTrial.gov (NCT04397575). In accordance with French regulatory laws, all analysed patients were informed and those not agreeing for the use of their clinical data were excluded.

2.2 Patients

The inclusion criteria were patients with a histologically confirmed solid malignant tumour and a diagnosis of COVID-19. Patients undergoing anticancer treatments or treated curatively more than five years previously were excluded. The diagnosis of COVID-19 was based on the confirmation of SARS-CoV-2 infection by quantitative RT-PCR on nasopharyngeal swabs, and/or imaging features consistent with COVID-19 pneumonia on CT-scan or based on highly suggestive symptoms combined with positive SARS-CoV-2 serology. Patients with suggestive symptoms of COVID-19 without a RT-PCR, CT-scan or serological confirmation during the study period were excluded from the analysis. Patients were included in the cohort on the basis of clinicians' reporting of all consecutive cases diagnosed at their center. The cut-off date for our study was June 12, 2020.

2.3 Data collection

The following data were collected by clinicians on an electronic Case Report Form: age, sex, geographical location of patients' residences, smoking status, body mass index (BMI), comorbidities with the updated Charlson Comorbidity Index (uCCI) [11], usual medication, type and status of cancer, Eastern Cooperative Oncology Group (ECOG) performance status (PS), anticancer therapy in the 4 weeks and in the 3 months before the COVID-19 diagnosis respectively, the course of the COVID-19 infection, complications and treatment, especially admission to hospital and/or intensive care unit (ICU), the need for supplemental oxygen and mechanical ventilation and death.

2.4 Outcomes

The primary endpoint was all-cause mortality following the diagnosis of COVID-19. Secondary outcomes were admission to hospital, admission to an ICU, the need for supplemental oxygen and the use of mechanical ventilation during the COVID-19, and the impact of COVID-19 on management of the cancer. The COVID-19 severity outcome was defined as admission to an ICU and/or use of mechanical ventilation and/or death.

2.5 Statistical analysis

Analyses compared patients who died with those still alive on June 11, 2020. Quantitative variables were described using the usual statistics: n , mean, standard deviation, median, interquartile range, minimum and maximum. Qualitative variables were described using numbers and percentages. Missing values were not counted for percentage calculations. For quantitative variables, groups were compared using a Student or Wilcoxon test and for qualitative variables, using a χ^2 test or a Fisher exact test.

Risk factors associated with death and their odds ratios (ORs) were analysed using a univariate logistic regression model. Multivariate regression was used to estimate ORs and 95% confidence intervals (CI) for each factor. Variables for the multivariate analysis were selected according to their significance in the univariate logistic regression ($P < 0.05$). The same analyses were done for COVID-19 severity. We used SAS version 9.4 for the statistical analyses. The tests were all two-sided with a 5% type one error.

3. Results

3.1 Clinical characteristics of patients and impact of COVID-19 on cancer treatment

From April 4 to June 11, 2020, 1,354 patients from 153 institutions were registered in the national cohort database. Among these patients, 1,289 met the inclusion criteria (Figure 1): 727 patients diagnosed with COVID-19 between March 1 and April 2 were included retrospectively; the remaining 562 patients were diagnosed after April 2 and included prospectively. The diagnosis of COVID-19 was made on the presence of detectable SARS-CoV-2 by RT-PCR on nasopharyngeal swabs in 952 (73.8%) patients (including 294 patients who also had images consistent with COVID-19 pneumonia on CT-scan), on only imaging features consistent with COVID-19 pneumonia on CT-scan in 317 (24.6%) patients and on history of highly suggestive symptoms combined with positive SARS-CoV-2 serology in 20 (1.6%) patients.

The participating institutions were spread over the entire country (Figure 2) and were general hospitals, university hospitals, private centres and comprehensive cancer centres, accounting for 31%, 28%, 25% and 16% of cases, respectively. The median follow-up from COVID-19 diagnosis was 34 days (95% CI: 32 –36).

Patient demographics are shown in Table 1. The median age was 67 years and 795 (62%) patients were male. Digestive cancers were the most common type of cancer (36%), followed by thoracic (24%) and breast (13%) cancers and 59% of patients had a metastatic disease. During the 3 months before the COVID-19 diagnosis, 755 (59%) patients had received a systemic anticancer treatment.

Eighty-two percent of patients experienced typical symptoms during the course of COVID-19. The most common symptoms were fever (52%), cough (37%) and fatigue (26%). Gastrointestinal symptoms were identified in 12%, anosmia or ageusia were present in only 4% and 3%, respectively. In total, 734 (65%) patients were admitted to hospital, of whom 110 (10%) were admitted to an ICU; 412 (42%) patients required oxygen and 49 (5%) mechanical ventilation.

In the overall cohort, only 107 (11%) patients had their anticancer treatment modified (drug withdrawal or change, modification of the time interval between drug administrations) preventively before the COVID-19 infection because of the pandemic context. However, the systemic anticancer treatment was interrupted or stopped following the diagnosis of COVID-19 in 431 (39%) patients (Table 2).

3.2 Patient outcome and risk factors for death and COVID-19 severity

With a median follow-up of 34 days, 370 (29%) patients had died. The death was attributable to COVID-19 in most patients (N = 322, 87%) and occurred after a median of 10 days (IQR: 5-24). As shown in Table 1, compared with survivors, patients who died were older, more likely to be male and to be current or former smokers, had more frequently comorbidities, long-term or recent corticosteroids (for another reason than COVID-19), angiotensin II antagonists (AIIA) or angiotensin converting enzyme inhibitor (CEI) and anticoagulant therapy as their usual medication. They also had a poorer ECOG PS and a higher proportion of metastatic disease, and were more likely to have undergone cytotoxic chemotherapy in the 4 weeks or 3 months before the COVID-19 diagnosis. The impact of immune checkpoint inhibitors or other anticancer treatment on the course of COVID-19 could not be analysed because of the relatively low percentage of patients given such treatments.

The association between prognostic parameters and all-cause mortality are shown in Supplementary Table 1 and Figure 3. In univariate analysis, age, sex, the ECOG PS, the updated Charlson comorbidity index, smoking status, thoracic primary tumour location, metastatic tumour stage, lung metastases, cytotoxic chemotherapy during the 3 months before the COVID-19 diagnosis, corticosteroids before the COVID-19 diagnosis, anticoagulant therapy, CEI or AIIA, and admission to an ICU were significantly associated with an increased risk of death. In the multivariate analysis sex, the ECOG PS, the uCCI and admission to an ICU remained statistically significant risk factors for death. Age, smoking status and corticosteroids before the COVID-19 diagnosis also showed a statistically non-significant increased risk of death. Importantly, the administration of cytotoxic chemotherapy in the 3 months before COVID-19 diagnosis was not associated with an increased risk of death.

Overall, 424 (33%) patients had a severe form of COVID-19 defined by admission to an ICU and/or mechanical ventilation and/or death but only 129 (9%) patients were admitted to ICU and/or had mechanical ventilation without death, that a majority of patients died without a previous admission to ICU or a mechanical ventilation. The association between prognostic parameters and COVID-19 severity are shown in Supplementary Table 2 and Figure 4. In univariate analysis, age, sex, the ECOG PS, the uCCI, smoking status, thoracic primary tumour location, metastatic tumour stage, lung metastases, cytotoxic chemotherapy during the 3 months before the COVID-19 diagnosis, corticosteroids before the COVID-19 diagnosis, anticoagulant therapy, and CEI or AIIA were significantly associated with COVID-19 severity. In the multivariate, sex, the ECOG PS, the uCCI, corticosteroids before the COVID-19 diagnosis and thoracic primary tumour location remained independent predictors of COVID-19 severity. Age was associated with a statistically non-significant increase in the risk of death either. Again, the administration of cytotoxic chemotherapy in the 3 months before COVID-19 diagnosis was not associated with COVID-19 severity.

When the multivariate analysis was restricted only to patients with RT-PCR-documented SARS-CoV-2 (n=952), ECOG PS, uCCI and ICU admission remained statistically significant risk factors for death, as were age, smoking status and cytotoxic chemotherapy administered within 3 months before the COVID-19 diagnosis (Supplementary Table 3). The ECOG PS and the uCCI were the only independent predictors of COVID-19 severity (Supplementary Table 4).

Discussion

After starting in December 2019 in Wuhan, China, the COVID-19 epidemic quickly spread to Europe in March 2020 and then to the rest of the world with a speed that shook saturated healthcare systems unprepared for such a pandemic. In the wake of a small Chinese study suggesting that patients with cancer had a high risk of severe respiratory complications related to SARS-CoV-2 infection and that patients with the highest risk were those who had received chemotherapy or surgery in the month preceding the infection [1], the medical community began to modify various practices in the treatment of cancer during the COVID-19 pandemic. The main objectives of these changes were to avoid very high-risk situations such as surgery or intensive cytotoxic chemotherapy and to minimise patients' exposure to SARS-CoV-2.

For these reasons, in France, the French health authority published on March 11, 2020 guidelines to protect patients with cancer against SARS-CoV-2 infection [12]. Then, another study in Wuhan reported that cancer patients who had received their last anti-cancer treatment during the 14 days before the diagnosis of COVID-19 had an increased risk of experiencing severe events [13]. In this context, international and national panels recommended delaying or suspending anticancer treatments, when feasible, thereby raising the issue of potential cancer progression [14-22]. We created a national multicentre cohort in order to better understand the risk factors for mortality and severity of COVID-19, particularly the impact of various anticancer treatments, in order to determine the best practices and to help clinicians in their decision-making, and to assess the impact of COVID-19 on anticancer treatments.

First, our results show that the mortality rate in cancer patients with COVID-19 is far higher (29%) than that in COVID-19 patients overall [23, 24]. To date, all studies that have included a significant number of cancer patients with COVID-19 have reported a mortality rate > 10%. However, this rate is very variable between studies [4-9, 25-28], ranging from 11-12% [5, 25, 28] to 28% in two studies, including the UK Coronavirus Cancer Monitoring Project (UKCCMP) cohort that included 800 patients [4, 8]. Of note, the highest mortality rate published to date (33%) comes from the international cohort of patients with thoracic cancers and COVID-19 (TERAVOLT) [26]. In our cohort, the 311 patients with thoracic cancer had a mortality rate of 36%, which was the highest mortality rate of all tumour locations. The variations in mortality rates observed between studies could be explained, in part, by disparities in the proportions of patients with significant comorbidities or poor PS and in the proportions of the different types of tumours, as well as differences in the use of intensive care resources. It may also depend on hospital admission criteria to secondary care. In some countries, like in the US, a lower threshold is likely to exist and mild or asymptomatic patients might be admitted. A plausible explanation for the high mortality rate observed in our

cohort is both its larger size, and the 'selection bias', leading to a greater likelihood of registering patients with adverse COVID-19 outcomes, while cancer patients with less severe infections may not have been included in our cohort since not consulting during this period of time. Thus, the patients included in the French cohort were mainly hospitalized patients with most often symptomatic COVID-19 and thus probably more severe. Similarly, it is possible that at the time of the analysis some information may have been missing, especially in cases of ambulatory care for diseases with a benign course. The relatively low rate of ICU transfer (10%) in our cancer patients compared to others studies [7, 9, 13, 27, 28] could be explained by a general ICU policy, since all ICU departments in areas of high COVID-19 incidence in France were overwhelmed at that period, with a lack of available ICU beds. Patients without severe comorbidities were thus prioritized for ICU admission, and cancer patients with their underlying comorbidities could have been excluded from intensive care. However similar rates of ICU transfer (7% and 10% respectively) have been reported in the UKCCMP and TERA-VOLT studies [8, 26], probably for the same reasons. Retrospectively, the relevance of such triage strategy raises an ethical question and one can legitimately wonder whether these policies should continue in the event of a second wave, during which a better organization of intensive care access is to be hoped for.

We confirm the risk factors for death that have already been reported in previous studies, such as male sex, the ECOG PS or the presence of comorbidities, including cardiovascular disease, hypertension or COPD [4, 6-9]. One point that remains unclear is the impact of cancer treatments on the severity of COVID-19 and its mortality. According to our analysis, the recent administration of cytotoxic chemotherapy was not a significant risk factor for death in the overall cohort but slightly increased the risk of death in the sub-population of RT-PCR positive patients, at the limit of significance (OR = 1.53 95%CI: 1.00- 2.34; $p = 0.05$). The results in the literature are very discordant in this regard. Two Chinese studies showed that recent cytotoxic chemotherapy was associated with increased mortality [6, 9]. However, more recent results from the two large cohorts of cancer patients in the UK and the US [7, 8] and from the TERA-VOLT cohort of patients with thoracic cancers [26] concluded that chemotherapy had no effect on COVID-19-related mortality. Added to these last data, our results suggest that chemotherapy should be continued in confirmed SARS-CoV-2-negative patients during the pandemic, without significantly endangering the patient, but this would need to be confirmed on larger series, encouraging us to promote collaborative projects pooling data from different cohorts.

As recently reported in the two cohorts in the UK and US [7, 8], we found no association between mortality and the recent administration of non-cytotoxic systemic anticancer treatments, whether immunotherapy, targeted therapy or hormone therapy. Immunotherapy did not worsen outcomes for patients with COVID-19 in other studies, including two studies dedicated to patients with thoracic cancer [26-28]. However, the role of immunotherapy as a risk factor or not for COVID-19 severity or mortality remains to be clarified given the contradictory data from two previous Chinese studies reporting an increased risk of death or of severe disease with recent immunotherapy [6, 25]. Recent case reports have suggested that it is safe to maintain targeted therapy with ALK/ROS1 tyrosine kinase inhibitors in NSCLC patients with asymptomatic SARS-CoV-2 interstitial pneumonia. This is important as there is a high risk of a cancer flare-up following discontinuation of such a treatment, with a rapidly progressive adverse cancer course leading to death [29].

One of the objectives of our cohort was to analyse the impact of a COVID-19 diagnosis on cancer treatment. We found that COVID-19 was responsible for a temporary or definitive interruption of cytotoxic chemotherapy in 39% of patients and a change in the chemotherapy regimen in 5% of cases. We do not have sufficient hindsight to measure the consequences of these therapeutic modifications, but in the future, it will be essential to determine whether COVID-19-related changes in treatment were responsible for faster cancer progression and shorter survival.

The GCO-002 CACOVID cohort has some limitations. First, the diagnosis of COVID-19 was mainly made by RT-PCR and/or CT-scan. Due to their limited availability in France during the early phase of the pandemic, RT-PCR were reserved for patients with suggestive symptoms and therefore not carried out systematically throughout the country, even in vulnerable populations. This, added to the estimated 20-30% of false-negatives, probably contributed not only to an underestimation of the number of patients with COVID-19, as it was recently demonstrated [30], but also to an overestimation of the proportion of severe forms of COVID-19 since included patients were necessarily symptomatic and/or hospitalized. As the first part of the cohort was retrospective, some data were missing, but the database completion rate was $\geq 85\%$ for the majority of the parameters. Finally, the study does not provide an estimate of COVID-19 prevalence in cancer patients since we do not yet have the total number of cancer patients followed during the study period.

Despite these weaknesses, the cohort has strengths. To our knowledge, it is the largest cohort of cancer patients with COVID-19 to date. It covers the entire national territory and perfectly reflects the epidemiology of SARS-CoV-2 infection in France since the geographic

distribution of cancer patients with COVID-19 is similar to that of all infected patients in the country, the most affected regions being Greater Paris, and the Northeast and Southeast of France.

In conclusion, this nationwide cohort indicates that mortality in cancer patients with COVID-19 is high and is associated with general characteristics of patients. Age Patients receiving corticosteroids before COVID-19 diagnosis and patients with thoracic cancers had also more severe COVID-19. We found no deleterious effects of recent cytotoxic chemotherapy, except in the subgroup of patients with PCR-detected SARS-CoV-2 RNA. This suggests that cytotoxic treatments should be continued in SARS-CoV-2-negative patients during the pandemic, without significantly endangering the patient although such recommendation deserves to be confirmed on larger series. In almost 40% of patients, the systemic anticancer therapy was interrupted or stopped after COVID-19 diagnosis. The impact of these interruptions on cancer evolution will be evaluated in the future, as well as the impact of social inequalities on the severity and management of COVID-19 infections.

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Conflict of interest

Pr Lièvre reports grants from Bayer Lilly, Merck and Novartis, personal fees from AAA, Amgen, Bayer, BMS, Celgene, HalioDx, Incyte, Ipsen, Lilly, Merck, Novartis, Pierre Fabre, Roche, Sandoz, Sanofi, Servier and non financial support from AAA, Amgen, bayer, Incite, Ipsen, Merck, Novartis, Pierre Fabre, Pfizer, Roche, Sandoz, Servier and Integragen outside of the submitted work.

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Figure legends

Figure 1: Consort diagram

Figure 2: Geographic distribution of cancer patients with COVID-19 and participating institutions

Figure 3: Forest plot of the multivariate analysis of factors associated with all-cause mortality in the overall cohort of 1289 cancer patients with COVID-19

Figure 4: Forest plot of the multivariate analysis of factors associated with COVID-19 severity outcome defined by admission to ICU and/or mechanical ventilation and/or death in the overall cohort of 1289 cancer patients with COVID-19

Appendix

List of investigators/Collaborators of GCO-002 CACOVID-19 cohort

Dr MOULIN Solenne (SAINT GRÉGOIRE Clinique privée Saint Grégoire - Recherche clinique) ; Dr LELEU Olivier (ABBEVILLE CH THORAX) ; LEPARREE Sylvie (ABBEVILLE CH THORAX) ; Dr GOASDOUE Henri (ABBEVILLE CH) ; Dr PIPROT Christine (ABBEVILLE CH Service de Médecine B) ; Dr TOURNEUR Gerald (ABBEVILLE CH) ; Dr BAYART Vincent (ABBEVILLE CH) ; LIGNIER Delphine (AMIENS CHU HÔPITAL SUD) ; Dr LACHAÏER Emma (AMIENS CHU HÔPITAL SUD) ; KHAMARI Marwa (AMIENS CHU HÔPITAL SUD) ; Dr COUTTE Alexandre (AMIENS CHU HÔPITAL SUD) ; SIEMBIDA Nicolas (AMIENS CHU HOPITAL SUD - Service de chirurgie digestive) ; Dr HOUESSINON Aline (AMIENS CHU HÔPITAL SUD) ; Pr REGIMBEAU Jean Marc (AMIENS CHU HOPITAL SUD - Service de chirurgie digestive) ; Pr CHAUFFERT Bruno (AMIENS CHU HÔPITAL SUD - Service d'Oncologie médicale) ; Dr MOREIRA Aurélie (AMIENS CHU HÔPITAL SUD) ; Dr HAUTEFEUILLE Vincent (AMIENS CHU HÔPITAL SUD - Service d'Hépto-gastro-entérologie) ; HEE Christine (AMIENS CHU HÔPITAL SUD) ; Dr BOONE Mathieu (AMIENS CHU HÔPITAL SUD) ; Dr BIHAN Céline (AMIENS CHU HÔPITAL SUD) ; CHIVE Emilie (AMIENS CHU HOPITAL SUD - Service de chirurgie digestive) ; POULET-POTRIQUIER Stéphane (AMIENS CHU HÔPITAL SUD) ; FAHEM Rachida (AMIENS CHU HÔPITAL SUD - Service d'Hépto-gastro-entérologie) ; Dr LUET Dominique (ANGERS CHU HÔTEL DIEU - Service d'HGE) ; Dr ROQUIN Guillaume (ANGERS CHU HÔTEL DIEU - Service d'HGE) ; Dr VITELLIUS Carole (ANGERS CHU HÔTEL DIEU - Service d'HGE) ; CORNET-TRICHEREAU Nathanaëlle (ANGERS CHU HÔTEL DIEU - Service d'HGE) ; Pr CAROLI-BOSC François-Xavier (ANGERS CHU HÔTEL DIEU - Service d'HGE) ; Dr THIROT-BIDAULT Anne (ANTONY CH HOPITAL PRIVE - service d'Oncologie) ; Dr ROPERT Stanislas (ANTONY CH HOPITAL PRIVE - service d'Oncologie) ; Dr GACHET - MASSON Julie (ANTONY CH HOPITAL PRIVE - service d'Oncologie) ; DEHAIS Mélanie (ANTONY CH HOPITAL PRIVE - service d'Oncologie) ; Dr L'HELGOUALC'H Gwen-Ael (ANTONY CH HOPITAL PRIVE - service d'Oncologie) ; ALI-MAHAMADOU Ibrahim (ANTONY CH HOPITAL PRIVE - service d'Oncologie) ; TALFI Safia (ARGENTEUIL CH VICTOR DUPOUY - USRC Unité de Soutien à la Recherche Clinique) ; Dr BELMONT Laure (ARGENTEUIL CH VICTOR DUPOUY - USRC Unité de Soutien à la Recherche Clinique) ; BENREZZAK Nasro (ARGENTEUIL CH VICTOR DUPOUY) ; DUBIEF Emeline (ARGENTEUIL CH VICTOR DUPOUY - USRC Unité de Soutien à la Recherche Clinique) ; Dr CONROY Guillaume (ARS LAQUENEXY CH METZ THIONVILLE MERCY) ; Dr DELIQUE Laurence (ARS LAQUENEXY CH METZ THIONVILLE MERCY) ; BASSO Maud (AUCH CH Hôpital Général d'Auch) ; Dr PONS Isabelle (AUCH CH Hôpital Général d'Auch - Service d'Oncologie) ; Dr SALIGNON Karine (AUCH CH Hôpital Général d'Auch - Service d'Oncologie) ; Dr VILLING Anne-Laure (AUXERRE CH GHT UNYON AUXERRE - Service d'Oncologie) ; MOUGENOT Emmanuelle (AUXERRE CH GHT UNYON AUXERRE - Service d'Oncologie) ; POREBSKI Cassandra (AUXERRE CH GHT UNYON AUXERRE - Service d'Oncologie) ; GUIATNI Asma (AUXERRE CH GHT UNYON AUXERRE - Service d'Oncologie) ; Dr CLOAREC Nicolas (AVIGNON CH HENRI DUFFAUT - Service d'Onco-Hématologie) ; Dr MINEUR Laurent (AVIGNON Clinique privée SAINTE CATHERINE - Service d'Oncologie Médicale) ; BOUCHAUD Marie (AVIGNON Clinique privée SAINTE CATHERINE) ; Dr DAVID Céleste (AVIGNON Clinique privée SAINTE CATHERINE) ; Dr PEYTIER Annie (BAYEUX CH Service de Gastroentérologie) ; Dr GRELETTY Thomas (BAYONNE CH COTE BASQUE) ; Dr AUDEMAR Franck (BAYONNE CH CÔTE BASQUE -Service d'HGE) ; VIGNES Emanuelle (BAYONNE CH COTE BASQUE) ; Dr MINNE Floriane (BAYONNE CH COTE BASQUE) ; GOLDZAK Guillaume (BAYONNE CH COTE BASQUE) ; HUYSMAN Fabienne (BEAUVAIS CH Service d'Oncologie médicale) ; Dr HOCINE Fayçal (BEAUVAIS CH Service d'Oncologie médicale) ; Dr LAKKIS Zaher (BESANCON CHU JEAN MINJOZ) ; Dr MANSI Laura (BESANCON CHU JEAN MINJOZ) ; Dr MEYNARD Guillaume (BESANCON CHU JEAN MINJOZ) ; Dr ALMOTLAK Hamadi (BESANCON CHU JEAN MINJOZ - Service d'Oncologie) ; Dr KLAJER Elodie (BESANCON CHU JEAN MINJOZ - Service d'Oncologie) ; Dr SUN XU-SHAN (BESANCON CHU JEAN MINJOZ) ; Dr MANSI Laura (BESANCON Clinique privée FRANCHE COMTE) ; Dr WASSELIN Julie

(BETHUNE CH Germon et Gauthier - Service de Gastroentérologie) ; Dr CATALA Pascale (BETHUNE CH Germon et Gauthier - Service de Gastroentérologie) ; MAZUY Claire (BETHUNE CH Germon et Gauthier - Service de Gastroentérologie) ; Dr VANDAMME Hélène (BETHUNE CH Germon et Gauthier - Service de Gastroentérologie) ; Dr PREVOST Jean-Briac (BEUVRY Clinique privée CENTRE PIERRE CURIE) ; Dr FADIN Aurélie (BEUVRY Clinique privée CENTRE PIERRE CURIE) ; Dr BASSON Laurent (BEUVRY Clinique privée CENTRE PIERRE CURIE) ; HUGUET Jean-Baptiste (BEZIERS CH CH BEZIERS) ; DOS SANTOS Emmanuelle (BEZIERS CH CH BEZIERS) ; JANY Bérangère (BEZIERS CH CH BEZIERS) ; Dr SAAD Alain (BEZIERS CH CH BEZIERS) ; Dr GOUTORBE Frédéric (BEZIERS CH CH BEZIERS) ; Dr OZIOL Eric (BEZIERS CH CH BEZIERS) ; Dr RAMDANI Mohamed (BEZIERS CH Service d'HGE) ; KADIRI Ouafae (BLOIS CH Service d'Onco-Hématologie) ; Dr GARBAY Delphine (BORDEAUX Clinique privée TIVOLI - Service Oncologie-Radiothérapie) ; HUET Clotilde (BORDEAUX Clinique privée TIVOLI) ; Dr GIROUX LEPRIEUR Etienne (BOULOGNE CHU AP-HP AMBROISE PARÉ) ; TENG Wen (BOULOGNE CHU AP-HP AMBROISE PARÉ) ; MONVOISIN Justine (BOULOGNE SUR MER CH DUCHENNE- Bâtiment Administratif) ; Dr ARNAUD COFFIN Patrick (BOURG EN BRESSE CH FLEYRIAT) ; ROUX Sylvie (BOURG EN BRESSE CH FLEYRIAT - UNITE RECHERCHE CLINIQUE) ; Dr ORFEUVRE Hubert (BOURG EN BRESSE CH FLEYRIAT) ; CHAGROS Mélanie (BOURG EN BRESSE CH FLEYRIAT) ; Dr PILLON Didier (BOURG EN BRESSE CH FLEYRIAT - Service d'HGE) ; RASSOUL Agathe (BREST CHU MORVAN) ; Dr POUREAU Pierre Guillaume (BREST CHU MORVAN - Institut de cancérologie) ; NOVELLO Cécile (BRON HCL PIERRE WERTHEIMER) ; Dr DUCRAY François (BRON HCL PIERRE WERTHEIMER) ; TROUBA Cécile (BRON HCL PIERRE WERTHEIMER) ; Dr BASTIT Vianney (CAEN CAC FRANÇOIS BACLESSE) ; Pr BABIN Emmanuel (CAEN CHU CÔTE DE NACRE) ; Dr THARIAT Juliette (CAEN CAC FRANCOIS BACLESSE - ORL) ; LEON Vincent (CAEN CHU CÔTE DE NACRE) ; Dr COURTECUISSE Anne-Catherine (CALAIS CH) ; VAMBRE Julie (CALAIS CH) ; Dr TACK Vincent (CALAIS CH) ; Dr DESAUW Christophe (CALAIS CH) ; Dr MENIAI Fatima (CALAIS CH) ; PERES Christina (CALAIS CH) ; Dr ESPARCIEUX Aurélie (CALUIRE ET CUIRE Clinique privée INFIRMERIE PROTESTANTE) ; PERRIER Hervé (CALUIRE ET CUIRE Clinique privée INFIRMERIE PROTESTANTE) ; DOUX Nathalie (CANNES CH Service Oncologie) ; Dr KAPHAN Régis (CANNES CH Service Oncologie) ; Dr ROQUES Bertrand (CHALLES LES EAUX Clinique privée MÉDIPOLE DE SAVOIE) ; Dr REBISCHUNG Christine (CHALLES LES EAUX Clinique privée MÉDIPOLE DE SAVOIE) ; Dr MILLE Dominique (CHALLES LES EAUX Clinique privée MÉDIPOLE DE SAVOIE) ; FERNANDES Gaëlle (CHALLES LES EAUX Clinique privée MÉDIPOLE DE SAVOIE) ; Dr ABDELLI Naceur (CHALONS EN CHAMPAGNE CH Service HGE) ; JOUSSET Natacha (CHAMBRAY LES TOURS Clinique privée POLE SANTE LEONARD DE VINCI) ; Dr COMBE Pierre (CHAMBRAY LES TOURS Clinique privée POLE SANTE LEONARD DE VINCI) ; Dr JONVEAUX Eric (CHARLEVILLE CH Service de Radiothérapie) ; Dr DUMONT Patrick (CHAUNY CHU Service d'oncologie) ; Dr KANAAN Marc (CHAUNY CHU Service d'oncologie) ; Berthelot Gras Corinne (CHAUNY CHU Service d'oncologie) ; PANIS Valérie (CHAUNY CHU Service d'oncologie) ; Dr KALUZINSKI Laure (CHERBOURG-EN-COTENTIN CH CHP DU COTENTIN - Service Oncologie Médicale) ; VENANT-VALERY Marjolène (CHERBOURG-EN-COTENTIN CH CHP DU COTENTIN- Département de recherche clinique) ; Dr LAM You-Heng (CHOLET CH Service Maladies de l'appareil digestif du Dr KAASIS) ; VALLEE Laura (CHOLET CH Service Maladies de l'appareil digestif du Dr KAASIS) ; Dr RIVIERE Frédéric (CLAMART Hopital militaire HIA PERCY - THORAX) ; DURAND Muriel (CLERMONT FERRAND CHU ESTAING) ; BENGHADID Dihya (CLERMONT FERRAND CHU ESTAING) ; VILLENEUVE Emilie (CLERMONT FERRAND CAC JEAN PERRIN) ; Dr HENTIC DHOME Olivia (CLICHY CHU AP-HP BEAUJON - Service d'HGE) ; Dr LAURENT Lucie (CLICHY CHU AP-HP BEAUJON) ; BOUNOUAR Zedjiga (CLICHY CHU AP-HP BEAUJON) ; Dr DE MESTIER Louis (CLICHY CHU AP-HP BEAUJON - Service de gastroentérologie) ; DUBOIS Jacqueline (COLMAR CH HOPITAUX CIVILS DE COLMAR) ; EYRIEY Magali (COLMAR CH HOPITAUX CIVILS DE COLMAR) ; Dr MOREAU Lionel (COLMAR CH HOPITAUX CIVILS DE COLMAR) ; Dr AHLE Guido (COLMAR CH HOPITAUX CIVILS DE COLMAR) ; Dr BELMONT Laure (COLOMBES CHU AP-HP LOUIS MOURIER) ; Dr DIB Baihas (COMPIEGNE Clinique privée POLYCLINIQUE

SAINT COME Service d'oncologie) ; Dr ALDABBAGH Kaïs (COMPIEGNE Clinique privée POLYCLINIQUE SAINT COME Service d'oncologie) ; DEGRIFFOLET Dominique (COMPIEGNE Clinique privée POLYCLINIQUE SAINT COME Service d'oncologie) ; Dr SEBBAGH Virginie (COMPIEGNE CH Service d'HGE) ; SEGHEZZI Jean-Christophe (COMPIEGNE CH Service d'HGE) ; Dr LOZACH-BRUGIRARD Marion (CORBEIL-ESSONNES CH SUD FRANCILIEN - Service Oncologie) ; MANDROU Julie (CORBEIL-ESSONNES CH SUD FRANCILIEN - Unité de Recherche Clinique) ; MAVIER Loubna (CORNEBARRIEU Clinique privée CÉDRES) ; HENNETIER Florence (COUDEKERQUE BRANCHE Clinique privée CLINIQUE DE FLANDRE) ; Dr WAGNER Jean-Philippe (COUDEKERQUE BRANCHE Clinique privée CLINIQUE DE FLANDRE) ; Dr CAROLA Elisabeth (CREIL CH GHPSO (Site de Creil) - Service d'oncologie) ; CHANDIRAKUMARAN Karthiga (CREIL CH GHPSO (Site de Creil) - Service d'oncologie) ; Dr LOUTSKI Sandrine (CREIL CH GHPSO Site de Creil) ; Dr COJEAN-ZELEK Isabelle (CRETEIL CH C.H.I.C - Service d'Oncologie-Radiothérapie) ; BOURAS Amina (CRETEIL CHU HENRI MONDOR - Service hépatologie) ; LACOUR Sandrine (CRETEIL CH C.H.I.C.) ; FROURA Fahem (CRETEIL CHU AP-HP HENRI MONDOR) ; BEN NADJI Hadjer (CRETEIL CHU AP-HP HENRI MONDOR) ; CATTELAINE Sophie (DECHY Clinique privée CENTRE LEONARD DE VINCI) ; Dr DARLOY Franck (DECHY Clinique privée CENTRE LEONARD DE VINCI) ; Dr JOLIMOY BOILLEAU Geneviève (DIJON Clinique privée Institut de cancérologie de Bourgogne GRReCC) ; MAISSIAT Cyrielle (DIJON Clinique privée Institut de cancérologie de Bourgogne GRReCC) ; Dr DARUT-JOUE Ariane (DIJON Clinique privée Institut de cancérologie de Bourgogne GRReCC) ; Dr LORGIS Véronique (DIJON Clinique privée Institut de cancérologie de Bourgogne GRReCC) ; CHARIFI-ALAOUI Ikram (DIJON CAC GF LECLERC) ; Pr GHIRINGHELLI François (DIJON CAC Service Oncologie Médicale) ; Dr DROUILLARD Antoine (DIJON CHU François Mitterrand - Service d'HGE) ; Dr CHAIX MARIE (DIJON CHU François Mitterrand - Service d'HGE) ; Pr MANFREDI Sylvain (DIJON CHU François Mitterrand - Service d'HGE) ; Pr LEPAGE Côme (DIJON CHU François Mitterrand - Service d'HGE) ; Dr GAGNAIRE Alice (DIJON CHU François Mitterrand - Centre de Coordination en Cancérologie (3C)) ; Dr LATOURNERIE Marianne (DIJON CHU François Mitterrand - Service d'HGE) ; JOURDAN Sofia (DIJON CHU François Mitterrand - Service d'HGE) ; PERROT Nora (DIJON CHU François Mitterrand - Service d'HGE) ; Dr FOLIA Mireille (DIJON CHU Hôpital François Mitterrand) ; Dr MINELLO Anne (DIJON CHU François Mitterrand - Service d'HGE) ; Dr JOUVE Jean-Louis (DIJON CHU François Mitterrand - Service d'HGE) ; Dr MANSI Laura (DOLE CH LOUIS PASTEUR) ; FERY Marielle (DOUAI CH) ; Dr LANDAU Alain (DREUX CH VICTOR JOUSSELIN - Service d'HGE) ; TALFI Safia (ERMONT Clinique privée CLINIQUE CLAUDE BERNARD - THORAX) ; Dr BELMONT Laure (ERMONT Clinique privée CLINIQUE CLAUDE BERNARD) ; Dr EVRARD Diane (FEROLLES ATTILLY Hopital Privé FORCILLES) ; Dr VALENZA Bruno (FREJUS CH FREJUS ST RAPHAEL - Service d'Oncologie) ; Dr PAITEL Jean-François (FREJUS CH FREJUS ST RAPHAEL - Service d'Oncologie) ; CHABLAIS Laetitia (FREJUS CH FREJUS ST RAPHAEL - Service d'Oncologie) ; Dr KREITMANN Thomas (GRASSE CH) ; Dr LANCYRY-LECOMTE Laurence (GRENOBLE Clinique privée GHM DANIEL HOLLARD - GYNECOLOGIQUE) ; MONARD Adrien (GRENOBLE Clinique privée GHM DANIEL HOLLARD - GYNECOLOGIQUE) ; Dr FAUGERAS Eve (GRENOBLE Clinique privée GHM DANIEL HOLLARD - UROLOGIE) ; BOUCHERET Paul (GRENOBLE Clinique privée GHM DANIEL HOLLARD - UROLOGIE) ; GLOMMEAU Cécile (GRENOBLE CHU GRENOBLE ALPES THORAX) ; TCHIKLADZE Christine (GRENOBLE CHU GRENOBLE ALPES THORAX) ; Dr GARNIER TIXIDRE Claire (GRENOBLE Clinique privée GHM DANIEL HOLLARD - GYNECOLOGIQUE) ; Dr LONG Jérôme (GRENOBLE Clinique privée GHM DANIEL HOLLARD - UROLOGIE) ; ZAIDI Manel (GRENOBLE CHU GRENOBLE ALPES THORAX) ; BOUCHERET Paul (GRENOBLE Clinique privée GHM DANIEL HOLLARD - GYNECOLOGIQUE) ; DELABARRE Véronique (GRENOBLE Clinique privée GHM DANIEL HOLLARD - UROLOGIE) ; MEYZENC Juliette (GRENOBLE CHU GRENOBLE ALPES THORAX) ; DELABARRE Véronique (GRENOBLE Clinique privée GHM DANIEL HOLLARD - GYNECOLOGIQUE) ; MONARD Adrien (GRENOBLE Clinique privée GHM DANIEL HOLLARD - UROLOGIE) ; FERRAND Loïc (GRENOBLE CHU GRENOBLE ALPES THORAX) ; Pr MORO-SIBILOT Denis (GRENOBLE CHU GRENOBLE ALPES THORAX) ; BOUHERET Paul (GRENOBLE Clinique privée GHM Institut DANIEL HOLLARD - Service d'Oncologie) ; Dr

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JACQUIN Jean-Philippe (SAINT PRIEST EN JAREZ CHU INSTITUT CANCEROLOGIQUE LUCIEN NEUWIRTH - Service d'Oncologie Médicale) ; Dr RAMIREZ Carole (SAINT PRIEST EN JAREZ CHU INSTITUT CANCEROLOGIQUE LUCIEN NEUWIRTH - Service d'Oncologie Médicale) ; Dr VALLARD Alexis (SAINT PRIEST EN JAREZ CHU INSTITUT CANCEROLOGIQUE LUCIEN NEUWIRTH - Service d'Oncologie et Radiothérapie) ; COLLARD Olivier (SAINT PRIEST EN JAREZ CHU INSTITUT CANCEROLOGIQUE LUCIEN NEUWIRTH - Service d'Oncologie Médicale) ; Dr MURON Thierry (SAINT PRIEST EN JAREZ CHU INSTITUT CANCEROLOGIQUE LUCIEN NEUWIRTH - Service d'Oncologie Médicale) ; Dr RIVOIRARD Romain (SAINT PRIEST EN JAREZ CHU INSTITUT CANCEROLOGIQUE LUCIEN NEUWIRTH - Service d'Oncologie Médicale) ; Dr GRABER Ivan (SAINT COLOMBE LES VIENNE Clinique privée TRENEL) ; Dr TRAGER MAURY Stéphanie (STAINS Clinique privée ESTREE) ; DUBOISSET Elodie (STAINS Clinique privée ESTREE) ; Dr AYLON UGARTE Jorge (STAINS Clinique privée ESTREE) ; RAMI Dalilia (STAINS Clinique privée ESTREE) ; SALER Christine (STRASBOURG Clinique privée STRASBOURG ONCOLOGIE LIBERALE - Service HGE) ; REINBOLT Manon (STRASBOURG CAC ICAN STRASBOURG - Recherche Clinique) ; Dr LE FEVRE Clara (STRASBOURG CAC ICAN Institut de Cancérologie de Strasbourg Europe) ; Dr BEN ABDELGHANI Meher (STRASBOURG CAC ICAN Strasbourg - Service d'Oncologie) ; Dr DOURTHE Louis-Marie (STRASBOURG Clinique privée STRASBOURG ONCOLOGIE LIBERALE - Service HGE) ; PERRUISSEAU-CARRIER Joffrey (STRASBOURG CHU HAUTEPIERRE) ; Dr NGUIMPI-TAMBOU Marlène (STRASBOURG CHU HAUTEPIERRE - Service d'HGE) ; BARRET Flavie (SURESNES CH FOCH) ; Dr DI STEFANO Anna Luisa (SURESNES CH FOCH) ; BALTHAZARD Annie (SURESNES CH FOCH) ; Dr MABRO May (SURESNES CH FOCH - Service d'Oncologie) ; VASSORD-DANG Camille (SURESNES CH FOCH) ; LE MARCHAND Mathilde (SURESNES CH FOCH) ; Dr VERGNIOL Julien (TALENCE CH MAISON SANTÉ PROTESTANTE) ; Dr PRIPON Iulia (TARBES CH BIGORRE - Service d'HGE) ; Dr DAEMAEGDT Axelle (TARBES CH BIGORRE) ; LATRY Vanessa (TARBES CH BIGORRE) ; LARRIEU Muna (THONON LES BAINS CH LEMAN) ; LANDRY Gaëlle (THONON LES BAINS CH LEMAN) ; TOUIHRI MAXIMIN Laetitia (THONON LES BAINS CH LEMAN) ; Dr DEL PIANO Francesco (THONON LES BAINS CH LEMAN) ; BARLET Agnès (TOULON CH SAINTES MUSSE) ; VERNISSE Mylène (TOULON CH SAINTES MUSSE HOPITAL - SERVICE DAM/UNITE DE RECHERCHE CLINIQUE) ; LAFOND Sophie (TOULON CH SAINTES MUSSE) ; GENIN Charline (TOULON CH SAINTES MUSSE HOPITAL - SERVICE DAM/UNITE DE RECHERCHE CLINIQUE) ; Dr SIBERTIN-BLANC Camille (TOULON CH SAINTES MUSSE - Service d'oncologie) ; Dr CHABRILLAC Emilien (TOULOUSE CAC ONCOPOLE - ORL) ; GREGOIRE Caroline (TOULOUSE CHU RANGUEIL) ; Pr VERGEZ Sébastien (TOULOUSE CAC ONCOPOLE) ; PANOUILLE Quentin (TOULOUSE CHU RANGUEIL) ; Pr GUIMBAUD Rosine (TOULOUSE CHU RANGUEIL - Service d'oncologie digestive) ; RICHA Floriane (TOURCOING CH GUSTAVE DRON CH - Service d'oncologie) ; Dr LEBELLEC Loïc (TOURCOING CH GUSTAVE DRON CH - Service d'oncologie) ; GOUNIN Sophie (TOURS CHU BRETONNEAU - Service d'HGE) ; Dr BUIRET Guillaume (VALENCE CH) ; BAUDIN Marine (VALENCE CH Service d'Oncologie Médicale) ; Dr HAMON Hervé (VALENCE CH Service d'HGE) ; Dr DESHORGUE Anne-Claire (VALENCIENNES CH) ; FERY Marielle (VALENCIENNES CH) ; Dr BARRASCOUT Eduardo (VALENCIENNES CH) ; LEGRAND Stéphanie (VALENCIENNES CH) ; Dr LAURIDANT Géraldine (VALENCIENNES Clinique privée DENTELLIÈRES) ; HOULZE Morgane (VALENCIENNES Clinique privée DENTELLIÈRES) ; CAMBULA Linda (VALENCIENNES CH) ; Dr LOPEZ Anthony (VANDOEUVRE LES NANCY CHU BRABOIS - Service d'HGE) ; FOUQUET Guillaume (VANDOEUVRE LES NANCY CHU BRABOIS - Service d'HGE) ; TOUABI Kahina (VANDOEUVRE LES NANCY CHU BRABOIS - Service d'HGE) ; Pr GERMAIN Adeline (VANDOEUVRE LES NANCY CHU BRABOIS - Service d'HGE) ; Dr GODBERT Benoît (VANTOUX Hopital Privé ROBERT SCHUMAN) ; VOIVRET Florence (VANTOUX Hopital Privé ROBERT SCHUMAN) ; Dr PERRIN Julie (VANTOUX Hopital Privé ROBERT SCHUMAN) ; Dr MANSI Laura (VESOUL CH PAUL MOREL) ; DA SILVA Rosa (VILLEJUIF CAC GUSTAVE ROUSSY) ; Dr BERNICHON Emilie (VILLEJUIF CAC GUSTAVE ROUSSY) ;

Figure 1: Consort diagram

Figure 2: Geographic distribution of cancer patients with COVID-19 and participating institutions

Figure 3: Forest plot of the multivariate analysis of factors associated with all-cause mortality in the overall cohort of 1289 cancer patients with COVID-19

Figure 4: Forest plot of the multivariate analysis of factors associated with COVID-19 severity outcome defined by admission to ICU and/or mechanical ventilation and/or death in the overall cohort of 1289 cancer patients with COVID-19

Table 1: Clinical features of the 1289 cancer patients with COVID-19

	All patients (N = 1289)	Patients who died (N = 370)	Patients who survived (N = 919)	P value
PATIENTS' CHARACTERISTICS				
Age, years				
Median (range)	67 (19-100)	70 (22-98)	66 (58-74)	<0.001
< 65	534 (42%)	121 (33%)	413 (45%)	<0.001
65-74	430 (33%)	137 (37%)	293 (32%)	
≥ 75	325 (25%)	112 (30%)	213 (23%)	
Sex				
Female	494 (38%)	113 (30%)	381 (41%)	<0.001
Male	795 (62%)	257 (70%)	538 (59%)	
Region of patient's residence[#]	N = 1261	N = 366	N = 895	
Northeast	995 (79%)	286 (78%)	709 (79%)	0.13
Southeast	100 (8%)	28 (8%)	72 (8%)	
Northwest	69 (5%)	26 (7%)	43 (5%)	
Southwest	75 (6%)	24 (6%)	51 (6%)	
Centre	22 (2%)	2 (1%)	20 (2%)	
BMI (kg/m²)	N = 1110	N = 347	N = 774	
Median (range)	24.3 (12.1-52.7)	23.9 (13.0-43.6)	24.6 (12.1-52.7)	0.20
< 18.5	101 (9.1%)	38 (11%)	63 (8%)	0.24
18.5 ≤ BMI < 25	515 (46%)	167 (48%)	348 (45%)	
25 ≤ BMI < 30	311 (28%)	82 (23%)	229 (30%)	
30 ≤ BMI < 35	137 (12%)	41 (12%)	96 (12%)	
35 ≤ BMI < 40	32 (3%)	10 (3%)	22 (3%)	
≥ 40	14 (1%)	6 (2%)	8 (1%)	
Obesity (BMI ≥ 30)	183 (16%)	57 (17%)	126 (16%)	0.96
Tobacco smoking status	N = 1079	N = 334	N = 745	
Never smoked	515 (48%)	126 (38%)	389 (52%)	<0.001
Former smoker	393 (36%)	149 (44%)	244 (33%)	
Current smoker	171 (16%)	59 (18%)	112 (15%)	

Comorbidities, n/total				
Congestive heart failure	95/1151 (8%)	45/349 (13%)	50/802 (6%)	< 0.001
Coronary insufficiency	99/1019 (8%)	45/328 (14%)	54/691 (8%)	0.0029
Chronic obstructive pulmonary disease	124/1020 (12%)	55/328 (17%)	69/692 (10%)	0.0019
Diabetes	241/1151 (21%)	84/349 (24%)	157/796 (20%)	0.08
Hypertension	529/1151 (46%)	189/349 (54%)	340/802 (42%)	0.0002
Number of comorbidities	N = 1289	N = 370	N = 919	
0	175 (14%)	21 (6%)	154 (17%)	
1	280 (22%)	48 (13%)	232 (25%)	<0.001
2	294 (23%)	87 (23%)	207 (22%)	
3	216 (17%)	79 (21%)	137 (15%)	
≥ 4	324 (25%)	135 (36%)	189 (21%)	
Updated Charlson comorbidity index	N = 932	N = 299	N = 633	
0-3	284 (30%)	56 (19%)	228 (36%)	<0.001
≥ 4	648 (70%)	243 (81%)	405 (64%)	
Usual medication*, N /total				
Long-term corticosteroids	131/1141 (11%)	51/344 (15%)	80/797 (10%)	0.02
Transient corticosteroids (ongoing or ≤ 4 weeks)	46/1011 (4%)	24/323 (7%)	22/688 (3%)	0.003
NSAIDs	40/1142 (3%)	17/345 (4.9%)	23/797 (2.9%)	0.08
Immunosuppressive therapy	35/1012 (3%)	11/324 (3%)	24/688 (3%)	0.94
CEI or AIIA	222/1143 (19%)	81/346 (23%)	141/797 (18%)	0.02
Anticoagulant therapy	358/1140 (31%)	141/344 (41%)	217 (796 (27%)	<0.001
HISTORY OF CANCER				
Cancer type	N = 1287	N = 370	N = 919	
Digestive ^a	470 (36%)	146 (39%)	324 (35%)	<0.001
Thoracic ^b	311 (24%)	113 (30%)	198 (22%)	
Gynaecological	252 (20%)	44 (12%)	208 (22%)	
Breast Cancer	173 (68.7%)	26 (59.1%)	147 (70.7%)	
Other gynaecological ^c	79 (31.3%)	18 (40.9%)	61 (29.3%)	
Head and neck	104 (8%)	22 (6%)	82 (9%)	
Central nervous system	65 (5%)	19 (5%)	46 (5%)	
Genitourinary	65 (5%)	21 (6%)	44 (5%)	

Dermatological	14 (1%)	3 (1%)	11 (1%)	
Others	6 (<1%)	2 (<1%)	4 (<1%)	
Cancer stage	N = 1285	N = 370	N = 915	
Metastatic	758 (59%)	252 (68%)	506 (55%)	<0.001
Localised	527 (41%)	118 (32%)	409 (45%)	
Time since cancer diagnosis	N = 1134	N = 343	N = 791	
< 1 year	597 (53%)	176 (51%)	421 (53%)	0.79
1-3 years	290 (25%)	92 (27%)	198 (25%)	
≥ 3 years	247 (22%)	75 (22%)	172 (22%)	
ECOG PS before COVID-19 diagnosis	N = 931	N = 294	N = 637	
0	182 (20%)	20 (7%)	162 (25%)	<0.001
1	365 (39%)	88 (30%)	277 (44%)	
2	247 (26%)	104 (35%)	143 (22%)	
3-4	137 (15%)	82 (28%)	55 (9%)	
Anticancer treatment during 4 weeks before COVID-19 diagnosis				
Systemic therapy	491 (38%)	151 (41%)	340 (37%)	0.202
cytotoxic chemotherapy	385 (30%)	126 (34%)	259 (28%)	0.03
immunotherapy	62 (5%)	22 (6%)	40 (4%)	0.23
targeted therapy	114 (9%)	28 (8%)	86 (9%)	0.31
hormone therapy	27 (2%)	5 (1%)	22 (2%)	0.23
local therapy, n/total				
radiotherapy	95/1262 (7%)	30/357 (8%)	65/905 (7%)	0.45
surgery	56/1289 (4%)	12/370 (3%)	44/919 (5%)	0.61
Anticancer treatment during 3 months before COVID-19 diagnosis				
Systemic therapy	755 (59%)	224 (61%)	531 (58%)	0.36
cytotoxic chemotherapy	577 (45%)	183 (49%)	394 (43%)	0.03
immunotherapy	110 (8%)	40 (11%)	70 (8%)	0.06
targeted therapy	181 (14%)	42 (11%)	139 (15%)	0.08
hormone therapy	57 (4%)	10 (3%)	47 (5%)	0.06
local therapy, N/total				

radiotherapy	133/1289 (10%)	48/370 (13%)	85/919 (9.2%)	0.047
surgery	56/1289 (4%)	12/370 (3%)	44/919 (5%)	0.22
COVID-19 TREATMENT				
Admission to hospital	734/1125 (65%)	291/341 (85%)	443/784 (57%)	<0.001
Admission to ICU	110/1125 (10%)	62/341 (18%)	48/784 (6%)	<0.001
Oxygen therapy	412/984 (42%)	208/316 (66%)	204/668 (31%)	<0.001
Mechanical ventilation	49/989 (5%)	27/320 (8%)	22/669 (3%)	0.0005

^a Digestive tumours: colorectal (N = 185, 14.3%), pancreas (N = 86, 6.7%), stomach (N = 50, 3.8%), esophagus (N = 42, 3.2%), liver (N = 34, 2.6%), others (digestive neuroendocrine, biliary tract, anus, peritoneum, small intestine, appendix, gastrointestinal stromal tumour, others) (N = 73, 5.7%).

^b thoracic tumours: non-small cell lung carcinoma (N = 233, 18%), small cell lung carcinoma (N = 26, 1.9%), mesothelioma and others (N = 52, 4%)

^c gynaecological tumours: ovary (N = 37, 2.8%), cervix (N = 17, 1.3%), endometrium (N = 15, 1.2%), others (N = 10, 0.7%)

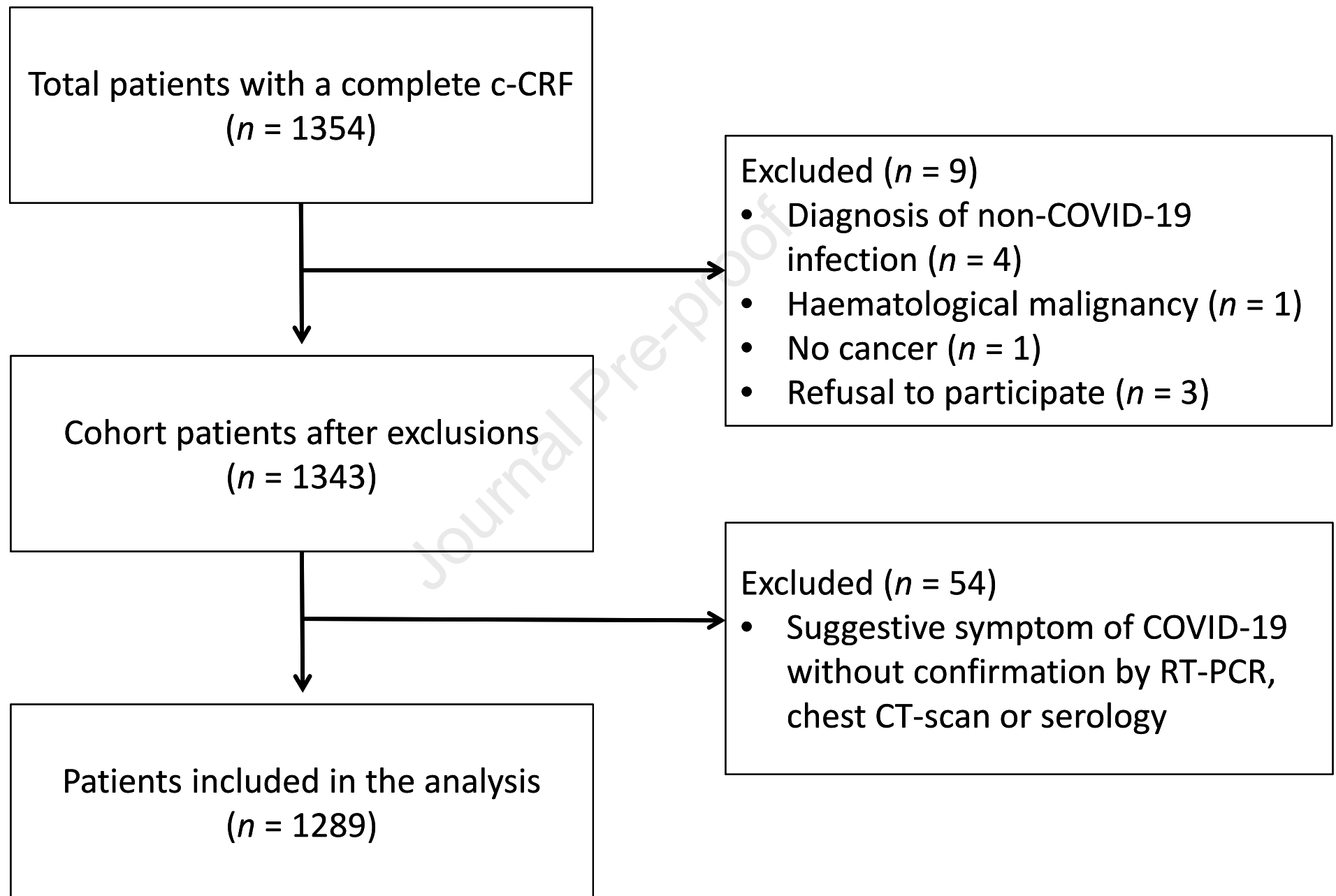
AIIA: angiotensin II antagonists, BMI: body mass index, CEI: converting enzyme inhibitor, NSAIDs: non-steroid anti inflammatory drugs, PS: performance status

* before COVID-19 diagnosis

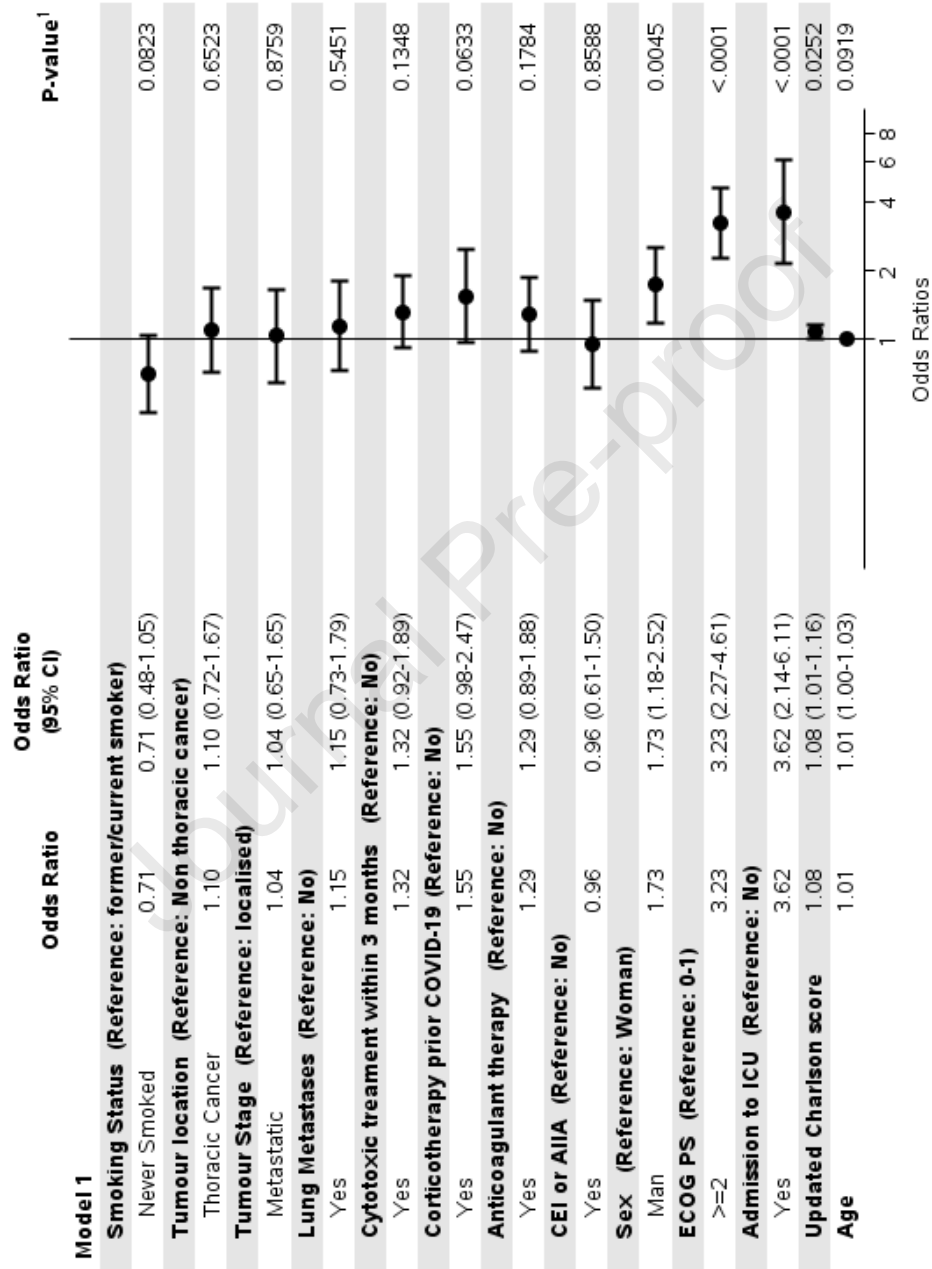
Northeast: Hauts-de-France, Paris/île-de-France, Grand-Est, Bourgogne-France-Comté; Southeast: Auvergne-Rhône-Alpes, Provence-Alpes-Côte d'Azur; Northwest: Normandie, Bretagne, Pays de la Loire; Southwest: Nouvelle-Aquitaine, Occitanie ; Centre : Centre-Val de Loire

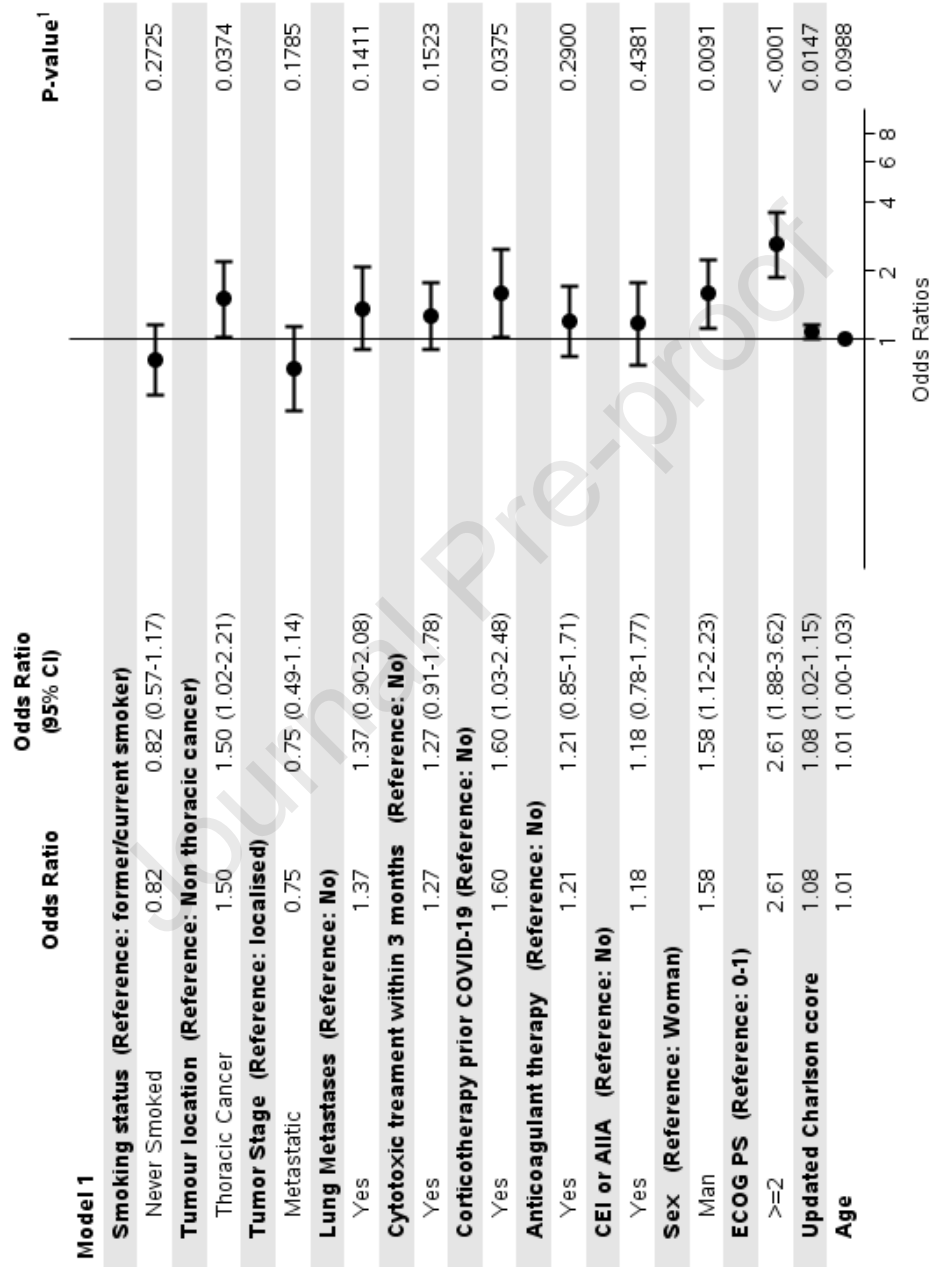
Table 2: Modification or interruption of anticancer treatments because of COVID-19 diagnosis

Anticancer treatment	Type of modification	Number (%)
Systemic therapy		N = 1092
	Modification of the regimen	53 (5%)
	Temporary interruption	321 (29%)
	Definitive interruption	110 (10%)
Radiotherapy		N = 1093
	Cancellation	1 (<1%)
	Modification of the radiation scheme	5 (<1%)
	Postponement	43 (4%)
	Definitive interruption	13 (1%)
Surgery		N = 1095
	Modification of the extent of surgery	1 (<1%)
	Cancellation	16 (2%)
	Postponement	24 (2%)
Interventional radiology		N = 1095
	Cancellation	2 (< 1%)
	Postponement	3 (<1%)





¹Covariate Wald p-value;



¹Covariate Wald p-value;

Highlights

- A total of 1289 patients with solid tumours and COVID-19 were analysed
- Mortality and COVID-19 severity were mainly driven by patient general characteristics.
- Overall, we found no deleterious effects of recent anticancer treatments on mortality.
- Systemic anticancer treatment was interrupted or stopped in 39% of patients

Declaration of interests

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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