COVID-19 mortality in hospitalized cancer patients is not significantly affected by chemotherapy or other anti-cancer treatments.

Abstract

Background

Individuals with cancer, particularly those who are receiving systemic anti-cancer treatments, have been postulated to be at increased risk of mortality from SARS-CoV-2 related coronavirus disease (COVID-19). This conjecture has considerable impact on the treatment of cancer patients and large, multi-centre data to support this assumption is lacking due to the contingencies of the pandemic.

Methods

The cancer community of the United Kingdom (UK) has launched the *UK Coronavirus Cancer Monitoring Project* (UKCCMP). The UKCCMP is the first COVID-19 clinical registry that enables near real-time reports to frontline doctors about the effect of COVID-19 on cancer patients.

Findings

An analysis of the first 800 cancer patients with symptomatic COVID-19 disease entered into the UKCCMP registry has been performed. Approximately half of these patients have a mild COVID-19 disease course (52%). Mortality was observed in 226 patients (28%) and risk of death was significantly associated with advancing patient age, sex (M>F) and the presence of other co-morbidities. Approximately one third had received cytotoxic chemotherapy within 4 weeks prior to testing positive for COVID-19. After adjusting for age, sex and comorbidities, recent receipt of chemotherapy had no significant effect on mortality from COVID-19 disease, when compared to cancer patients who had not received recent chemotherapy. No significant effect on mortality was also observed for patients with recent immunotherapy, hormonal therapy, targeted therapy or radiotherapy use.

Interpretation

Mortality from COVID-19 in cancer patients appears to be principally driven by age, sex and co-morbidities. We are not able to identify evidence that cancer patients on cytotoxic chemotherapy or other anti-cancer treatment are at significantly increased risk of mortality from COVID-19 disease compared to those not on active treatment.

Introduction

It is clear from data arising from the Office for National Statistics that the risk of morbidity and mortality from COVID-19 disease as a consequence of SARS-CoV-2 infection is not uniform across the population. Cancer patients on systemic anti-cancer treatments have been generally assumed by many to be at a higher risk than their counterparts who are not currently receiving anti-cancer treatment. The evidence to support this claim is scanty and limited to retrospective series arising from China, the epicentre of the current pandemic, and involving very small numbers of patients. [1,2,3] However despite these severe limitations, the promulgation of this hypothesis has led to widespread, global changes to chemotherapy and anti-cancer treatment prescribing patterns. [4] In a global health emergency, it is critical that oncologists secure evidence from a larger dataset, which can then inform their risk benefit analyses for individual patients in terms of the use of anti-cancer treatments. [5,6]

On 18th March 2020, we launched the *UK Coronavirus Cancer Monitoring Project* (UKCCMP) with widespread support across our national cancer network. [7,8] Within 5 weeks the UKCCMP had generated the largest prospective database and interrogation of COVID-19 disease in cancer patients generated to date. Here we describe the clinical and demographic characteristics and COVID-19 outcomes in this cohort of patients with cancer and symptomatic COVID-19 and attempt to assess how the presence of cancer and the receipt of cytotoxic chemotherapy and other anti-cancer treatments impacts upon COVID-19 disease phenotype.

Methods

Study Design and Participants

The UKCCMP database of United Kingdom (UK) cancer patients with a COVID-19 infection was launched with the support of the UK oncology professional bodies, including the *Association of Cancer Physicians (ACP), The Royal College of Radiologists (RCR),* the *National Oncology Trainees Research Collaborative for Healthcare Research (NOTCH),* patient support groups including *Macmillan Cancer Support,* charities including *Action Radiotherapy* and our national research body, *Cancer Research UK (CRUK).* [9,10] It was designed as a Public Health Surveillance registry to support rapid clinical decision-making, in accordance with the UK Policy Framework for Health and Social Care Research, the UK National Research Ethics Service and the UK Governance Arrangement for Research Ethic Committees. At an institutional level, this cohort study was approved according to local information governance processes. All patients with active cancer and presenting to our network of cancer centres from March 18th 2020 to April 26th 2020 with COVID-19 were eligible for enrolment into the UKCCMP. In keeping with international practice, patients were deemed to have COVID-19 if there was a positive SARS-CoV-2 Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) assay test from a throat/nose swab. Patients with a radiological or clinical diagnosis of COVID-19, without a positive RT-PCR test were not included in this analysis. As such, these patients are, by definition, symptomatic, requiring secondary care review for potential hospitalization. They were not part of a proactive surveillance program. 'Patients with active cancer' was defined as those with metastatic cancer, or on anti-cancer treatment in any setting (curative/radical/adjuvant/neoadjuvant setting) or treated within the past 12 months with surgery/cytotoxic chemotherapy/radiotherapy. Stage of tumour was divided into those into those that were *Primary Tumour Localized*- localized to organ and therefore potentially resectable, *Primary Tumour- locally advanced*- where it had spread locally from the primary organ and not resectable, *Metastatic*- where there is distant spread (stage 4) and those presently in *Remission*. Patients were assessed as to whether they had received chemotherapy (which did not include denosumab), immunotherapy, hormonal therapies or radiotherapy within 4 weeks of contraction of SARS-CoV-2. Non-palliative chemotherapy was defined as chemotherapy that was used in a neoadjuvant/adjuvant/radical setting. For the purposes of the present analysis, outcomes were monitored up to April 26th 2020.

Data Collection

Prospective data collection was performed by the newly formed pan-UK cancer centre emergency response network. Case reporting was led by a COVID-19 Emergency Response Reporting Individual (ERRI), supported by a Local Emergency Response Reporting Group (LERRG) at each centre. The role of the LERRG was to ensure near continuous reporting of cases in situations of absence of the ERRI due to off-days, illness, compassionate leave, self-isolation or re-deployment. The UKCCMP encouraged all local reporting sites to enter data in a real time basis, as soon as a positive SARS-CoV-2 test had been identified. The data fields were then re-updated as soon as treatment and outcomes had been identified and also to reflect the worse COVID-19 severity scores during hospitalization. The ERRI was a trained/in training oncologist who performed data review, annotation and entry. In a small number of centres, data entry was performed by data managers but with direct oversight by the ERRI. All registry entries were de-identified at source to ensure data anonymity to researchers. Data was entered into a Research Electronic Data Capture (REDCap) browser-based metadata driven electronic data capture (EDC) software system. [11] This secure EDC platform is hosted by the Institute of Translational Medicine at the University of

Birmingham. Patient demographics, treatment details, COVID-19 disease course and cancer features were obtained from the direct assessment of the ERRI/LERRG and/or through hospital medical records. COVID-19 Severity Score was determined according to the WHO guidelines.[12] Cancer type was defined according to ICD-10 diagnostic codes.

UKCCMP data processing and analysis

The data through the REDCap platform is transferred securely through to the Compute and Storage for Life Science (CaStLeS) infrastructure as part of the Birmingham Environment for Academic Research local Cloud (BEARCloud) [13] at the Centre for Computational Biology, University of Birmingham.

Within CaStLeS, the data is curated to avoid duplications and errors, then annotated with further information such as geolocation before it can be analysed and disseminated. The deployment of an automatic workflow, with human-in-the-loop, enables near real-time robust data analytics delivery to oncology medical health professionals through a weekly report in addition to a secured interactive web portal. Importantly, it enables delivery of national and local analytics with dynamic level of granularity.

Statistical analysis & Data visualisation

In this study, we report on the clinical outcomes of cancer patients who developed COVID-19 disease, assessing whether the patient died or eventually achieved discharge, and observing the effect of anti cancer treatment on outcomes. The two-sided Welch's t-test was used to compare continuous data and two-sided Fisher's exact test was used to compare categorical data from different categories with multivariate Bonferroni (multi-test) adjustment. A primary endpoint of all-cause mortality was defined *a priori*. This included deaths described as related to COVID-19 during this admission, as well as deaths reported as a consequence of any other cause during this admission, such as due to cancer progression or treatment toxicity. This was used for all regression analyses. Multivariate analyses were performed in SPSS, version 26 and Fisher's Exact tests in R version 3.6.3 utilising the Fisher.test () function. Multivariable logistic regression was used to estimate odd ratios and 95% confidence intervals of each factor after adjustment for clinically relevant potential confounders of age, sex, diabetes, hypertension, COPD or other comorbidities at admission. Goodness of fit was checked using Hosmer-Lemeshow test and, unless otherwise reported, had $p>0.05$. Where this goodness of fit criteria was not met, further multivariable logistic regression models using the above potential confounders was performed using a forward selection of $p<0.10$. Patients with either 'no information/missing relevant data' were not included in these regression analyses. Sub-group analyses of patients on chemotherapy was performed in order to better identify risk in this cohort of patients. This included an analysis of non-palliative vs. palliative chemotherapy, first line vs. later lines of palliative chemotherapy, palliative chemotherapy vs. no anti-cancer treatment, palliative chemotherapy vs. no recent chemotherapy. The justification for these analyses is that the cancer chemotherapy group is heterogenous. These subgroup analyses have a well-established oncology/clinical rationale, for example, non-palliative (curative) chemotherapy aims to prevent recurrence or eradicate disease, whereas palliative chemotherapy aims to maintain quality of life, or extend life usually by a matter of months, and both patient and chemotherapy treatment (drugs, dose and intensity) necessarily evolve as a patient progresses from 1st line to later lines of chemotherapy. [14] Data processing and visualisation utilised R (version 3.6.3) packages.

Project funding

This project was funded by the University of Birmingham (data collection and time of JPC, LL, UKCCMP and GM) and the University of Oxford (RK time). The University of Birmingham had no formal role in data collection, analysis, interpretation or decision to submit.

Results

Fifty-five Cancer centres had appointed a COVID-19 local emergency response reporting group (LERRG) and form part of this clinical network of cancer centres. Together this network covered a patient population of nearly 1.5 million patients who were living with active cancer with good coverage across all regions of the United Kingdom (Figure 1).

This early patient cohort consists of the first 800 patients with active cancer who had a documented SARS-CoV-2 infection presenting as symptomatic COVID-19 disease. As presented in Table 1, 56% of patients were male with a median age of 69.0 years (IQR 59-76). Comorbidities were common, including hypertension (n=247, 31%), diabetes (n=131, 16%), cardiovascular disease (n=109, 14%), COPD (n=61, 8%). One hundred and sixty-nine cancer patients were listed as having no comorbidities apart from their cancer diagnosis (21%). Approximately half of the patients had current ongoing metastatic cancer (n=347, 43%), of which malignant neoplasia of the digestive organs (n=150, 19%), haematological malignancies (n=109, 14%), breast (n=102, 13%) and respiratory and thoracic organs (n=90, 11%) were the commonest primary tumour sites. The median time from identification of documented COVID-19 disease until study end points were met (death or discharge from hospital) was 5 days (range 0-38).

In terms of the pattern of COVID-19 presentation, most presented with fever (n=484, 61%), cough (n=377, 47%), and/or shortness of breath (n=312, 39%). However, diarrhoea (n=51, 6%), nausea and vomiting (n=39, 5%), ageuisa (n=13, 2%) and anosmia (n=9, 1%) were also identified as less common presenting symptoms.

A number of correlates of severity of COVID-19 were measured, according to WHO criteria. [12] A mild COVID-19 severity was score was recorded in 412 patients (52%), with 96 patients (12%) not requiring hospitalization. 315 patients required oxygen (39%), and 53 patients received ITU-level care (7%). Of these 53 patients, at the time of analysis, 6 were discharged (11%), 23 died (43%) and 24 were either still in ITU and/or did not have a final recorded outcome (45%). The ITU admission rate was notably low and reflective of findings from the UK intensive care national audit and research centre (ICNARC) [15].

Death in this cohort was the final outcome in 226 patients (28%) with reporting stating that the death was principally attributable to COVID-19 in the majority of these cases (n=211 (93%). This mortality rate is higher than reported literature in the ‘general’ population, and likely to reflect the relative severity of symptoms of cancer patients who seek help from secondary care. Compared to the rest of the cancer cohort, patients who died were significantly older (median 73.0 years vs. 66.0 years, $p<0.001$) (Figure 2), more were male (mortality 33% 146/449) than female (mortality 23% 80/349) and those who died also displayed higher rates of comorbidities including cardiovascular disease (21% vs 11%, $p<0.001$) and hypertension (41% vs 27%) ($p<0.001$). They were also more likely to present with symptoms of shortness of breath (57% vs 32%) ($p<0.001$).

Across the cohort, 22% of patients were reported by sites as having their anti-cancer treatments interrupted due to the COVID-19 pandemic, however, the exact nature of this interruption is unknown.

Compared to patients who had not received chemotherapy within 4 weeks of testing positive for COVID-19, those who had received recent chemotherapy did not suffer increased mortality when analysed by univariate analysis (27% death rate with chemotherapy vs 29% death rate without recent chemotherapy).

In order to explore this relationship in greater detail, an in-depth analysis of the 281 patients who had received recent chemotherapy use was therefore performed (Figure 3). There were no significant differences in underlying cancer primary site in the recent chemo versus no chemo group. However, compared to cancer patients who had not received recent chemotherapy, the chemotherapy positive cohort was younger (median age 64.0 years vs. 71.0 $p<0.001$). Therefore, a multivariate analysis with adjustment for age, sex and comorbidities was performed and we found that deaths in COVID-19 cancer patients who had received recent chemotherapy were still no more likely than those that had not (OR 1.18, 95% CI [0.81 to 1.72]; p=0.380) (Table 2). However, this analysis had a borderline fit (Hosmer-Lemeshow test p value=0.048). To be more confident of our findings, we also performed a forward regression model (Hosmer-Lemeshow goodness of fit p=0.476) with similar findings (OR 1.15, 95% CI [0.79 to 1.66], p=0.467). We specifically explored the interaction of chemotherapy and disease severity and this interaction term is not significant in predicting mortality (OR 1.16, 95% CI [0.42 to 3.19], p=0.768). This was not significant and is not included in the final model.

Patients receiving chemotherapy are a heterogeneous group and so further exploratory subgroup analyses were performed. On further multivariate analysis of the group of patients who had received recent chemotherapy, decreased odds of death was found in patients receiving non-palliative chemotherapy (neoadjuvant/adjuvant/radical) compared to those receiving palliative chemotherapy (16% vs 35%) (OR 0.40 CI [0.17 to 0.96]; p=0.040) following adjustments for age, sex and comorbidities. However, the odds of death in these palliative chemotherapy patients was still not significantly different to cancer patients with no anti-cancer treatment at all (OR 1.05, 95% CI [0.63 to 1.76]; p=0.854), but there was a non-significant trend compared to those with no recent chemotherapy (OR 1.48, 95% CI [0.93 to 2.36]; p=0.102). There was no significant differences in mortality in those patients receiving first line palliative chemotherapy compared to those receiving later lines of palliative treatment (OR 0.84, 95% CI [0.36 to 1.98]; p=0.690) following adjustments for age, sex and comorbidities.

Finally, we analysed the use of other forms of anti-cancer therapies within 4 weeks of testing positive for SARS-CoV-2 infection and presenting with COVID-19 disease. Compared to the rest of the cohort who were not on these therapies, patients on immunotherapy (n=44, OR 0.59, 95% CI [0.27 to 1.27]; p=0.177), hormonal therapy (n= 64, OR 0.90, 95% CI [0.49 to 1.68]; p=0.744), radiotherapy (n=76, OR 0.65, 95% CI [0.36 to 1.18]; p=0.159) and targeted therapies (n= 72, OR 0.83, 9% CI [0.45 to 1.54]; p=0.559) were also not at any additional risk of death following adjustment for age, sex and comorbidities (Figure 4).

Discussion

Global healthcare systems are currently dealing with the COVID-19 pandemic, a disease caused by SARS-CoV-2 infection; a situation which is set to be a generational challenge to all clinicians. At the time of writing, the clinical phenotype and interactions of SARS-CoV-2 infection/ COVID-19 disease with pre-existing disease and systemic anti-cancer treatments agents is poorly described and based on very small retrospective studies.

The disruption from the pandemic to normal oncological care has been huge for a number of reasons. Firstly, cancer clinicians and the rest of the cancer team are under unprecedented pressures, with increasing concern from patients about their perceived 'vulnerability', cancelled cancer operations, a significant drive to do telemedicine rather than face to face consultations, and a high degree of absence from work across the cancer team, due to personal illness and self / household isolation. Secondly, many oncologists are being redeployed to general or acute medicine roles to support the large number of COVID-19 admissions requiring intensive medical support and input. Thirdly, a couple of small studies reporting COVID-19 outcomes in cancer patients has resulted in the community being fearful of giving effective anticancer treatments. These studies concluded that cancer patients are not only more susceptible to contracting the virus, but also at risk of developing more severe sequelae.[3,2] In the largest cohort of 105 cancer patients consisting of only 17 on chemotherapy, 6 patients on immunotherapy and 4 on targeted therapies, strong recommendations were made about the COVID-19 risk from anti-cancer treatments.[1] All of these studies are small cohorts and limited to a very restricted number of cancer centres. We felt that the studies raised important hypotheses but were in no way unequivocal and indeed there are contradictory studies from single centre studies from the United States of America. [16] To clarify the relationship between cancer, anti-cancer treatments and COVID-19 infection, it is clear that larger-scale datasets are necessary.

Because of the limited prevalence of the coexistence of cancer and COVID-19 disease, individual health care centres and physicians will only encounter small numbers of patients with both diseases. In addition, because of the fire-fighting nature of pandemic healthcare, much of the usual infrastructure of medical professional data dissemination has been completely dismantled: local, national, and international clinical meetings have been delayed or cancelled as part of public health measures to prevent COVID-19 spread. It is therefore of even greater importance that national and international strategies to share data quickly and effectively are created during this time of unprecedented need for rapid learning and evidence regarding best practice.

The UKCCMP was designed to serve as a Public Health Surveillance registry to answer important questions about the interaction of cancer, its treatments and COVID-19, and to support rapid clinical decision-making. Close alignment of healthcare systems, physicians, and patients has meant that the project was launched and produced clinically meaningful output over the course of four weeks.

In this paper, the UKCCMP describes the demographics of cancer patients with COVID-19 and explores the effect of cytotoxic chemotherapy and other anti-cancer treatments on the trajectory of that disease. We have identified that the phenotype of diagnosed COVID-19 disease in over half of cancer patients is mild, but death from COVID-19 in this cohort was observed in a significant percentage of patients. This mortality is higher than that observed in the general non-cancer UK population, [17] and may be reflective

of the severity of symptoms of the cancer patients who choose to seek treatment in secondary healthcare setting. It is interesting to note that the rate of admission to ITU was low at about 6% compared to a death rate of approximately 28%. Our dataset is currently unable to answer the question as to whether this might arise as a result of advance patient healthcare directives, hospital/ITU admission policy, a reluctance of treating physicians to utilise ITU resources for cancer patients or historically lower numbers of ITU beds available in the United Kingdom [18]. This does raise questions as to whether having a diagnosis of cancer decreases the potential access of these patients to the most intensive support.

From this early dataset, using multivariate analysis, we conclude that cytotoxic chemotherapy given within 4 weeks prior to confirmed COVID-19 disease is not a significant contributor to a more severe disease or a predictor of death from COVID-19, compared to cancer patients who have not received chemotherapy in that period. Whilst numbers are smaller, similar observations were observed for immunotherapy, hormonal therapy, targeted therapy and radiotherapy. Again, further interrogation with higher numbers will allow us to confirm or refute this finding.

Overall, in interpreting these data, and putting them into context, we suggest that it is important to continue to shield cancer patients from exposure to SARS-CoV-2, though self-isolation, minimising hospital visits where they can be avoided (which may mean a substitution or more oral agents in place of intravenous drugs), avoiding the mixing of COVID negative and COVID positive workstreams within the hospital environment; and by mitigating the risk of neutropenia to avoid the risk of simultaneous COVID-19 and bacterial septicaemia. It is also important to ensure that cancer patients have equivalent access to ITU care. However, in answer to the frequent question from patients as to whether chemotherapy or anti-cancer treatments will increase their risk of dying from COVID-19, in addition to the increased risk due to their cancer, our answer should be, not necessarily so. In patients presenting to NHS trusts or cancer centres, our data is strongly indicative that cancer COVID-19 mortality is principally driven by advancing age and the presence of other non-cancer co-morbidities. We conclude that withholding effective cancer treatments from significant numbers of cancer patients during the current pandemic runs the very real risk of increasing cancer morbidity and mortality, perhaps much more so than COVID-19 itself.

It is important to note the current limitations of the UKCCMP. Our analysis is partly dependent on the UK national COVID-19 testing policy, which is currently is less permissive than other nations [19,20] and also relies on RT-PCR which has a well described false negative result. [21] The project may therefore underreport total COVID-19 cases in cancer patients, particularly those with no/mild symptoms and who do not require or present to healthcare centres. On the other hand, because we are in such close and frequent contact with our patients, and have a high index of suspicion on their behalf, we may also repeat testing and potentially over report SARS-CoV-2 infection compared to the general population. One might argue that there could be a selection bias, in that those patients that were *not* on chemotherapy may have been taken off because of a poorer performance status, thus increasing their risk of death from COVID-19 disease, and reducing our ability to assess the real risk of anticancer treatments in a better performance status 'healthier' population. However, we have attempted to address this through multivariate analyses with age and co-morbidity correction. Finally, we do not comment on overall incidence of COVID-19 positivity amongst cancer patients because we do not yet have secure numerators and denominators for that calculation. However, total number of cases remain thankfully low, likely reflecting effective cancer social isolation policies.

Despite these noted limitations, the UKCCMP is unique in covering the majority of the UK cancer population, with universal access to cancer care and has been achieved through the rapid set up of a dedicated and coordinated emergency cancer network. The UKCCMP will continue to update our data weekly and share our outcomes with the oncological community.

With greater numbers analysed we will be able to answer more nuanced questions and guide further research. It will be important to investigate if the grading of COVID-19 could be further refined, to add granularity to our understanding the heterogeneity between different tumour subtypes, to clarify the risks of specific anti-cancer treatments, to determine if there are risks relating to more specific timing of anti-cancer treatments, and to gain a better understanding of the interaction between the host immune response and risk from COVID-19. There are some very interesting questions surrounding the differential impact of various anticancer treatments on different components of the immune system (neutrophils, cyototoxic T-cells, regulatory T cells and macrophages) and how these will interplay with the risk of contracting SARS-CoV-2 infection, or with the possibility of severe COVID-19 disease sequelae such as the cytokine storm.

Table 1: Clinical features of patients in the UKCCMP registry, 16th April 2020, with breakdown by all- cause mortality. Data are displayed as number of cases, except for age which is median age.

Patient features	All patients (n=800)	Patients Died (n=226)	Patients Survived (n=574)
Sex and age			
- Male	449 (56%)	146 (65%)	303 (53%)
- Female	349 (44%)	80 (35%)	269 (47%)
- Other[a]	2 (0%)	0 (0%)	2 (0%)
- Median age/years	69	73	66
Co-morbidities			
- Cardiovascular disease	109 (14%)	48 (21%)	61 (11%)
- COPD	61 (8%)	24 (11%)	37 (6%)
- Diabetes	131 (16%)	46 (20%)	85 (15%)
- Hypertension	247 (31%)	92 (41%)	155 (27%)
- None	169 (21%)	27 (12%)	142 (25%)
- Other[b]	336 (42%)	108 (48%)	228 (40%)
- No information	123 (15%)	28 (12%)	95 (17%)
Cancer type			
- Lip, oral cavity and pharynx	27 (3%)	4 (2%)	23 (4%)
- Digestive organs	150 (19%)	42 (19%)	108 (19%)
- Respiratory and intrathoracic organs	90 (11%)	32 (14%)	58 (10%)
- Melanoma (Skin)	27 (3%)	4 (2%)	23 (4%)
- Breast	102 (13%)	18 (8%)	84 (15%)
- Female genital organs	45 (6%)	5 (2%)	40 (7%)
- Male genital organs	78 (10%)	30 (13%)	48 (8%)
- Urinary tract	50 (6%)	16 (7%)	34 (6%)
- Central nervous system	15 (2%)	3 (1%)	12 (2%)
- Lymphoma	60 (8%)	20 (9%)	40 (7%)
- Other Haematological	109 (14%)	40 (18%)	69 (12%)
- Other[c]/unspecified	47 (6%)	12 (5%)	35 (6%)
Cancer Stage			
- Primary Tumour - Localised	149 (19%)	40 (18%)	109 (19%)
- Primary Tumour - Locally Advanced	78 (10%)	14 (6%)	64 (11%)
- Metastatic	347 (43%)	103 (46%)	244 (43%)
- Remission	21 (3%)	3 (1%)	18 (3%)
- No information	205 (25%)	66 (29%)	139 (24%)
Cancer treatment within 4 weeks			
- Chemotherapy	281 (35%)	75 (33%)	206 (36%)
- Hormone Therapy	64 (8%)	21 (9%)	43 (7%)
- Immunotherapy	44 (6%)	10 (4%)	34 (6%)
- Radiotherapy	76 (10%)	18 (8%)	58 (10%)
- Surgery	29 (4%)	7 (3%)	22 (4%)
- Targeted Treatment	72 (9%)	16 (7%)	56 (10%)
- Other[d]	60 (8%)	13 (6%)	47 (8%)
- None	272 (34%)	92 (41%)	180 (31%)
- No information	10 (1%)	1 (0%)	9 (2%)
COVID-19 Severity Score			
- Mild	412 (52%)	22 (10%)	390 (68%)
- Severe	187 (23%)	59 (26%)	128 (22%)
- Critical	173 (22%)	140 (62%)	33 (6%)
- No information	28 (3%)	5 (2%)	23 (4%)
COVID-19 treatment			
- ITU	53 (7%)	23 (10%)	30 (5%)

[a] Patient features- other, identifies patient where the patient does not identify as either male/female
[b] Co-morbidities- other, identifies co-morbidities which are not any of the co-morbidities included in the tables
[c] Cancer type- other, identifies ICD10 cancer types including malignant neoplasia of the bone and articular tissue, endocrine glands, mesothelioma and soft tissue and any other tumour type which was not included in the table.
[d] Cancer type- other, identifies cancer treatments which do not fall into the cancer treatment types defined in the table

Table 2: Regression analysis and odds of death based on features of patients in the UKCCMP. Univariate analysis was conducted with presence compared to absence (reference) for each category except for sex and age. Male sex was compared with reference to female sex. A Bonferroni p-value adjustment was performed. Multivariate analysis was conducted correcting for age, sex and patient co-morbidities.

Patient features	Univariate analysis Odds Ratio (95% CI)	*p value*	*p adjusted*	
Sex and age				
- Sex	1.67 (1.19-2.34)	0.003	0.006	**
- Age	9.42 (6.56-10.02)	<0.0001	<0.0001	****
Co-morbidities				
- Cardiovascular disease	2.32 (1.47-3.64)	0.0003	0.0019	**
- COPD	1.80 (1.00-3.27)	0.063	ns	
- Diabetes	1.61 (1.03-2.48)	0.032	ns	
- Hypertension	1.95 (1.36-2.80)	0.0003	0.0015	**
Cancer type				
- Lip, oral cavity and pharynx	0.42 (0.13-1.21)	0.116	ns	
- Digestive organs	0.91 (0.60-1.38)	0.680	ns	
- Respiratory and intrathoracic organs	1.50 (0.91-2.45)	0.121	ns	
- Melanoma (Skin)	0.37 (0.12-1.14)	0.079	ns	
- Breast	0.48 (0.28-0.84)	0.009	ns	
- Female genital organs	0.31 (0.11-0.81)	0.010	ns	
- Male genital organs	1.99 (1.14-3.48)	0.015	ns	
- Urinary tract	1.10 (0.58-2.12)	0.745	ns	
- Central nervous system	0.64 (0.15-2.32)	0.760	ns	
- Lymphoma	1.30 (0.71-2.30)	0.373	ns	
- Other Haematological	1.57 (1.01-2.42)	0.040	ns	
Cancer Stage				
- Primary Tumour - Localised	1.04 (0.67-1.64)	0.912	ns	
- Primary Tumour - Locally Advanced	0.58 (0.29-1.09)	0.111	ns	
- Metastatic	1.34 (0.90-2.01)	0.145	ns	
- Remission	0.42 (0.10-1.43)	0.204	ns	
Cancer treatment within 4 weeks				
- Chemotherapy	0.78 (0.55-1.11)	0.173	ns	
- Hormone Therapy	1.16 (0.64-2.06)	0.659	ns	
- Immunotherapy	0.60 (0.27-1.24)	0.179	ns	
- Radiotherapy	0.66 (0.37-1.17)	0.178	ns	
- Surgery	0.83 (0.32-2.15)	0.825	ns	
- Targeted Treatment	0.56 (0.30-1.01)	0.058	ns	
COVID-19 Severity Score				
- Mild	0.03 (0.02-0.05)	<0.0001	<0.0001	****
- Severe	1.63 (1.10-2.40)	0.015	0.045	*
- Critical	89.65 (41.64-209.83)	<0.0001	<0.0001	****
COVID-19 treatment				
- ITU	1.95 (1.09-3.52)	0.027	0.027	*

Treatment features	Multivariate analysis Odds Ratio (95% CI)	*p value*
Recent ant-cancer treatments		
- Chemotherapy vs no chemotherapy	1.18 (0.81-1.72)	0.380
- Hormone therapy vs no hormone Therapy	0.90 (0.49-1.68)	0.744
- Immunotherapy vs no Immunotherapy	0.59 (0.27-1.27)	0.177
- Radiotherapy vs no radiotherapy	0.65 (0.36-1.18)	0.159
-Targeted treatment vs no targeted treatment	0.83 (0.45-1.54)	0.559
Cytotoxic Chemotherapy		
-Non-palliative chemo vs palliative chemo	0.40 (0.17-0.96)	0.040
-Palliative 1st line chemo vs other line	0.84 (0.36-1.98)	0.690
-Palliative chemo vs no chemo	1.48 (0.93-2.36)	0.102
-Palliative chemo vs no treatment	1.05 (0.63-1.76)	0.854

* *denotes statistical significance of p adjusted, where* * p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

Acknowledgements

The authors thank the oncologists, acute physicians and healthcare staff working tirelessly on the frontlines of the COVID-19 pandemic.

We would like to thank Prof David Adams, Pro-Vice Chancellor and the Institute of Cancer and Genomic Sciences, University of Birmingham, for giving support and approval for this project.

We would like the thank the following Emergency Response Reporting Individuals, Abigail Gault, Agnieszka Michael, Alec Maynard, Ali-Abdulnabi Mohamed, Alison Massey, Amy Kwan, Annet Madhan, Ashley Poon King, Barlomiej Kurec, Caroline Dobeson, Caroline Usbourne, Clair Brummer, , Sinclair, Hayley Boyce, Hayley McKenzie, Heather Shaw, James Best, Joseph Sacco, Joseph Chacko, Laura Feeney, Lauren Cammaert, Leena Mukherjee, Madhumita Bhattacharyya, Mark Baxter, Martin Scott-Brown, Matthew Fittall, Michael Rowe, Mohammed Alhilali, Oliver Topping, Omar Shekh, Pauline Leonard, Peter Hall, Pippa Corrie, Rebecca Lee, Rebecca Sargent, Robert Goldstein, Roderick Oakes, Rohan Shotton, Ruth Board, Samah Massalha, Sangary Kathirgamakartgigeyan, Saoirse Dolly, Sean Brown, Shawn Ellis, Shefali Parikh, Siam Pugh, Simon Grumett, Stephanie Cornthwaite, Tom Roques, Yvette Drew, Victoria Brown and Victoria Woodcock.

Author Contributions

The following authors were involved in the study design (LL, RK, GM), data collection (LL, JBC, GM, RK, UKCCMP), analysis (LL, JBC, TS, CT, RK, GM), interpretation (LL, JBC, TS, CT, RK, GM), writing of manuscript (LL, JBC, TS, CT, RK, GM) and decision to submit (LL, JBC, CT, TS, RK, GM).

LL-Lennard Lee, JBC-Jean-Baptiste Cazier, TS-Thomas Starkey, CT-Chris Turnbull, UKCCMP-UK Coronavirus Cancer Monitoring Project, RK-Rachel Kerr, GM-Gary Middleton

The UK Coronavirus Cancer Monitoring Project (UKCCMP) was delivered by the work of Vasileios Angelis, Roland Arnold, Naomi Campton, Jean-Baptiste Cazier, Jaishree Bhosle, Vinton Cheng, Julia Chackathayil, Helen Curley, Matthew Fittall, Luke Freeman-Mills, Spyridon Gennatas, Paul Greaves, Daniel J Hughes, David Kerr, Rachel Kerr, Alvin Lee, Lennard YW Lee, Pauline Leonard, Sophie McGrath, Gary Middleton, Nirupa Murugaesu, Alicia Okines, Anna Olsson-Brown, Claire Palles, Yi Pan, Ruth Pettengell, Tom Powles, Karin Purshouse, Shivan Sivakumar, Thomas Starkey, Chris Turnbull, Csilla Varnai, Nadia Yousaf.

Declaration of interest

Dr Anna Olsson has received honoraria from BMS and Roche and research funding as part of a MRC fellowship (Roche, Eli Lily, UCB Pharma and Novartis). Dr Shivan Sivakumar is funded as a clinician-scientist as part of a Celgene Translational Fellowship. The other authors have no interest to declare.

REFERENCES

1. Dai, M.-Y. *et al. Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multi-Center Study During the COVID-19 Outbreak*. https://papers.ssrn.com/abstract=3558017 (2020) doi:10.2139/ssrn.3558017.
2. Liang, W. *et al.* Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol.* **21**, 335–337 (2020).
3. Yu, J., Ouyang, W., Chua, M. L. K. & Xie, C. SARS-CoV-2 Transmission in Patients With Cancer at a Tertiary Care Hospital in Wuhan, China. *JAMA Oncol.* (2020) doi:10.1001/jamaoncol.2020.0980.
4. Oncology, T. L. COVID-19: global consequences for oncology. *Lancet Oncol.* **21**, 467 (2020).
5. Haar, J. van de *et al.* Caring for patients with cancer in the COVID-19 era. *Nat. Med.* 1–7 (2020) doi:10.1038/s41591-020-0874-8.
6. Saini, K. S. *et al.* Effect of the COVID-19 pandemic on cancer treatment and research. *Lancet Haematol.* **0**, (2020).
7. Anil, I. *et al.* The UK Coronavirus Cancer Monitoring Project: protecting patients with cancer in the era of COVID-19. *Lancet Oncol.* **0**, (2020).
8. UK Coronavirus Cancer Monitoring Project. *UK Coronavirus Cancer Monitoring* https://ukcoronaviruscancermonitoring.com/.
9. Coronavirus Project Supporters. *UK Coronavirus Cancer Monitoring* https://ukcoronaviruscancermonitoring.com/supporters/.
10. COVID-19: Open letter to cancer researchers. *Cancer Research UK* https://www.cancerresearchuk.org/funding-for-researchers/research-features/2020-04-06-covid-19-open-letter-to-cancer-researchers (2020).
11. Harris, P. A. *et al.* Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *J. Biomed. Inform.* **42**, 377–381 (2009).
12. Wu, Z. & McGoogan, J. M. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA* **323**, 1239–1242 (2020).
13. Thompson, S. J., Thompson, S. E. M. & Cazier, J.-B. CaStLeS (Compute and Storage for the Life Sciences): a collection of compute and storage resources for supporting research at the University of Birmingham. (2019) doi:10.5281/zenodo.3250616.
14. *Skeel's Handbook of Cancer Therapy*. (Lippincott Williams and Wilkins, 2016).
15. ICNARC – About. https://www.icnarc.org/Our-Audit/About.

16. Miyashita, H. *et al.* Do Patients with Cancer Have a Poorer Prognosis of COVID-19? An Experience in New York City. *Ann. Oncol.* **0**, (2020).
17. COVID-19: track coronavirus cases. *GOV.UK* https://www.gov.uk/government/publications/covid-19-track-coronavirus-cases.
18. Rhodes, A. *et al.* The variability of critical care bed numbers in Europe. *Intensive Care Med.* **38**, 1647–1653 (2012).
19. Coronavirus testing in Europe, by country 2020. *Statista* https://www.statista.com/statistics/1109066/coronavirus-testing-in-europe-by-country/.
20. Coronavirus Disease (COVID-19) – the data. *Our World in Data* https://ourworldindata.org/coronavirus-data.
21. Comparative accuracy of oropharyngeal and nasopharyngeal swabs for diagnosis of COVID-19. *CEBM* https://www.cebm.net/covid-19/comparative-accuracy-of-oropharyngeal-and-nasopharyngeal-swabs-for-diagnosis-of-covid-19/.
22. Boundaries in the United Kingdom. NUTS Level 1 (January 2018). http://geoportal.statistics.gov.uk/datasets/nuts-level-1-january-2018-full-clipped-boundaries-in-the-united-kingdom.

FIGURE LEGENDS

Figure 1: Geographical plot, 26th April 2020, demonstrating the prevalence of COVID-19 in the Scotland, Wales and regions of England. Data displayed is average number of cases from reports per cancer centre region.

Figure 2: Horizontal bar plot demonstrating the age distribution of cancer patients in the cohort and relation to patient mortality.

Figure 3: Sankey plot demonstrating relationship of chemotherapy use within 4 weeks of contracting COVID-19 infection and mortality and severity of disease course. The vertical coloured bars denote the patient cohort, split into different groups (purple- severity of COVID19, blue- presence or absence of recent chemotherapy, red/green-patient mortality). The grey horizontal bars denote that associations between the different groups with wider bars denoting more overlap.

Figure 4: Forest plots showing effect of anti-cancer treatments and mortality from COVID-19 infection

Supplementary Methods

Data visualisation and figure generation

Data processing and visualisation utilised R (version 3.6.3) packages including broom, dplyr, gpclib, ggmap, ggplot2, mapdata, maps, maptools, networkD3, rgdal, rgeos, robustbase and viridis. Data subsetting was performed using the subset() function of 'robustbase' and data reshaping for visualisation involved the use of the group_by() and melt() functions of 'dplyr'. Functions from the ggplot2 R package were used to generate multiple plots including barplots (geom_bar) and UK region map (geom_polygon). The sankeyNetwork() function of the 'networkD3' R package was also used to generate the Sankey plot. The shape (.shp) file for the UK region map was publicly available from the UK Office for National Statistics. [22]