



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Original Research

Coronavirus disease 2019 in patients with neuroendocrine neoplasms: Preliminary results of the INTENSIVE study



Nicola Fazio ^{a,*}, Lorenzo Gervaso ^{a,b}, Thorvardur R. Halfdanarson ^c, Anna La Salvia ^d, Johannes Hofland ^e, Jorge Hernando ^f, Mohamad B. Sonbol ^g, Rocio Garcia-Carbonero ^d, Jaume Capdevila ^f, Wouter W. de Herder ^e, Anna Koumarianou ^h, Gregory Kaltsas ⁱ, Maura Rossi ^j, Simona Grozinsky-Glasberg ^k, Kira Oleinikov ^k, Sabrina Boselli ^l, Darina Tamayo ^l, Vincenzo Bagnardi ^m, Alice Laffi ^a, Manila Rubino ^a, Francesca Spada ^a

^a Division of Gastrointestinal Medical Oncology and Neuroendocrine Tumors, European Institute of Oncology (IEO) IRCCS, Milan, Italy

^b Molecular Medicine Program, University of Pavia, Pavia, Italy

^c Division of Medical Oncology Mayo Clinic, Rochester, MN, USA

^d Medical Oncology Department, Hospital Universitario Doce de Octubre, Imas12, UCM, Madrid, Spain

^e Department of Internal Medicine, Sector Endocrinology, Rotterdam, the Netherlands

^f Vall Hebron University Hospital and Vall Hebron Institute of Oncology (VHIO), Barcelona, Spain

^g Department of Hematology and Oncology Mayo Clinic, Phoenix, AZ, USA

^h Hematology-Oncology Unit, Fourth Department of Internal Medicine, Attikon Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece

ⁱ 1st Department of Propaedeutic Internal Medicine, Endocrine Unit, National and Kapodistrian, University of Athens, 11527 Athens, Greece

^j Oncology Unit and Centro Documentazione Osteonecrosi, Azienda Ospedaliera SS Antonio e Biagio e Cesare Arrigo, Alessandria, Italy

^k Neuroendocrine Tumors Unit, ENETS Center of Excellence, Department of Endocrinology and Metabolism Service, Hadassah-Hebrew University Medical Center, Jerusalem, Israel

^l Data Management-Clinical Trial Office. Scientific Direction. European Institute of Oncology (IEO) IRCCS, Milan, Italy

^m Department of Statistics and Quantitative Methods, University of Milan-Bicocca, Milan, Italy

Received 6 June 2021; accepted 16 June 2021

Available online 30 June 2021

KEYWORDS

Neuroendocrine

Abstract *Background:* Specific data regarding coronavirus disease 2019 (COVID-19) in patients with neuroendocrine neoplasms (NENs) are lacking. The aim of this study is to describe

* Corresponding author: Division of Gastrointestinal Medical Oncology and Neuroendocrine Tumors, European Institute of Oncology, Via G. Ripamonti 435, 20141, Milan, Italy. Fax: +390294379224.

E-mail address: nicola.fazio@ieo.it (N. Fazio).

<https://doi.org/10.1016/j.ejca.2021.06.029>

0959-8049/© 2021 Elsevier Ltd. All rights reserved.

neoplasms;
Neuroendocrine
tumours;
COVID-19;
SARS-CoV-2;
Coronavirus

the characteristics of patients with NENs who tested severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) positive.

Material and methods: This is a worldwide study collecting cases of patients with NENs along with a positive nasopharyngeal swab reverse transcriptase-polymerase chain reaction (RT-PCR) test for SARS-CoV-2 between June 1, 2020, and March 31, 2021. Centres treating patients with NENs were directly contacted by the principal investigator. Patients with NENs of any primary site, grade and stage were included, excluding small-cell lung carcinoma and mixed adenoneuroendocrine carcinoma.

Results: Among 81 centres directly contacted, 88.8% responded and 48.6% of them declined due to lack of cases or interest. On March 31st, 2021, eight recruiting centres enrolled 89 patients. The median age was 64 years at the time of COVID-19 diagnosis. Most patients had metastatic, non-functioning, low-/intermediate-grade gastroenteropancreatic NENs on treatment with somatostatin analogues and radioligand therapy. Most of them had comorbidities. Only 8% of patients had high-grade NENs and 12% were receiving chemotherapy. Most patients had symptoms or signs of COVID-19, mainly fever and cough. Only 3 patients underwent sub-intensive treatment, whereas most of them received medical therapies, mostly antibiotics. In two third of cases, no changes occurred for the anti-NEN therapy. More than 80% of patients completely recovered without sequelae, whereas 7.8% patients died due to COVID-19.

Conclusions: Patients included in this study reflect the typical NEN population regardless of SARS-CoV-2. In most cases, they overcome COVID-19 without need of intensive care, short-term sequelae and discontinuation of systemic oncological therapy.

© 2021 Elsevier Ltd. All rights reserved.

1. Introduction

Coronavirus disease 2019 (COVID)-19 is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that emerged in Wuhan, China, in late 2019 and rapidly spread all over the world causing a pandemic [1].

On 30 December 2019, a previously unknown beta-coronavirus was identified from the bronchoalveolar lavage of a patient with pneumonia of unknown aetiology by using RT-PCR in Wuhan Jinyintan Hospital [2]. This new coronavirus, named 2019-nCoV, was later named SARS-CoV-2 owing to its association with severe acute respiratory syndrome. The related disease, mainly involving the respiratory system, initially was named COVID-19. Information on the epidemic was notified to the World Health Organisation (WHO) on 3 January 2020. After that, the outbreak spread outside China, and on 30 January 2020, the WHO declared COVID-19 as the sixth public health emergency of international concern. On 11 March 2020, the WHO general director, Dr Tedros Adhanom Ghebreyesus, declared that the SARS-CoV-2 outbreak could be characterised as a pandemic. Thus far, the pandemic has resulted in a large number of excess deaths compared with recent years [3].

As patients with cancer have historically been considered to bear higher risk of infection and related complications, largely secondary to the immunosuppressive effects of the malignancies and the cancer-directed therapies, the main oncological societies published general

guidance to aim patients with cancer on their websites. Moreover, an international collaborative group proposed some practical measures for the management of patients with cancer based on the available data [4].

It was also reported that patients with cancer are more susceptible to viral infections, particularly those related to SARS-CoV-2 [5]. Furthermore, according to data originating from a Chinese cohort, patients with cancer had a significantly higher risk of developing severe COVID-19-related events, mainly intensive care unit (ICU) admissions, compared with patients without cancer (39% vs 8%, $p = 0.0003$) [6]. A higher COVID-19 mortality rate has also been reported in patients with cancer compared with those without cancer [7–11]. Multiple other studies have reported high mortality rates in patients with cancer who acquired COVID-19 [11–13].

In line with this, some types of cancers, including thoracic cancers, and clinical underlying conditions, such as concomitant immunosuppressive concurrent therapies and/or immune-related comorbidities, put patients with cancer at a higher risk for infection and complications of COVID-19 [14,15]. However, patients with different cancer types have different susceptibility to SARS-CoV-2 infection and COVID-19 phenotypes [16].

Based on the aforementioned considerations, it is not clear where and how to locate patients with neuroendocrine neoplasms (NENs) within this context. They represent a rare and heterogeneous group of malignancies, and their clinical behaviour, response to treatment and prognosis can be very different. Most patients

with metastatic disease receive a form of systemic oncological treatment from somatostatin analogues (SSAs) to intensive chemotherapy that can increase the risk of viral infections. Therefore, global recommendations from scientific societies about management of patients with NENs during the COVID-19 pandemic should consider all these differences.

However, currently there are no available data regarding the risk of infection, disease status and complications of patients with NENs during the COVID-19 pandemic, although several consensus articles have been published reporting some general recommendations [17–21].

We searched PubMed on April 05, 2021, using the search terms ('novel coronavirus' OR 'SARS-CoV2' OR 'COVID-19') AND ('neuroendocrine tumors' OR 'neuroendocrine tumours' OR 'neuroendocrine neoplasms' OR 'neuroendocrine carcinomas' OR 'carcinoids') for articles in English that documented COVID-19 in patients with NENs. Sixteen articles appeared, including three case reports, 12 recommendations or consensus statements and one only mini-series of four cases among a large thoracic cancer series [17–20,22–33].

Therefore, based on the rarity of patients with NENs, we conducted a worldwide collection of data through an international database to characterise the clinical course of patients with NENs and COVID-19. This study aims to generate a large data set to evaluate the frequency of events, clinical management and outcomes and demographic, geographical and biological correlations of patients with NENs and COVID-19 infection. This could help the clinical and scientific community and also the healthcare policies to guide the management of patients with NENs during the COVID-19 pandemic and design future clinical approaches in this setting.

At the date of the data-lock analysis of this manuscript (31 March 2021), more than 126 million total confirmed cases of COVID-19 have been recorded all over the world, from 223 countries, resulting in 2,800,000 deaths [34].

2. Patients and methods

This is a retrospective/prospective, observational, international, multicentric study on consecutive patients with NENs positive for SARS-CoV-2. Established centres known to be involved in national or international NEN clinical networks or European Neuroendocrine Tumor Society (ENETS) Centers of Excellence (CoE) were directly invited by email to join this study. After obtaining permission from local institutional review boards (IRBs), data were uploaded in a web application (REDCap) which reported the clinical characteristics of patients with NENs and COVID-19.

The protocol was approved by the IRB of the European Institute of Oncology (IEO) that is also the

coordinating centre in June 2020 and subsequently registered on clinicaltrials.gov (INTENSIVE [InterNational rEgistry oN Sars-cov-2 posItiVe nEuroendocrine neoplasm patients]; NCT04444401). Local IRB approval was required for each centre before data entry. The study includes patients with defined eligibility criteria from January 2020 until the end of the pandemic.

Eligible patients had to have NENs of any primary site, grade and stage with a positive SARS-CoV-2 swab test (RT-PCR), could be asymptomatic or presenting symptoms/signs of COVID-19 and being on active NEN treatment, with macroscopic evidence of NEN or with no evidence of NEN (if they received surgical ± locoregional non-surgical treatments within the last 2 months from the SARS-CoV-2 infection). Patients with NENs and symptoms suggestive of COVID-19 who did not undergo SARS-CoV-2 swab tests (RT-PCR) were excluded. Patients with small-cell lung cancer or non-pure NEN (e.g. MiNEN) were also excluded.

2.1. Statistical analysis

Descriptive statistics were used to summarise patient characteristics. To evaluate the association between age, sex and type of NENs with the risk of death, the non-parametric test for trend and the Fisher exact test were used for ordinal and nominal variables, respectively.

3. Results

For this initial analysis, data from consecutive patients entered into the database between June 01, 2020, and March 31, 2021, with complete reports, were collected.

Other than the IEO, 81 total centres were directly contacted by the principal investigator of the study. Among 24 Italian (IT) and 57 non-IT centres, representing 39 countries and five continents, nine centres did not respond (88.8% response rate) Fig. 1. Of the 72 responding centres, 35 (48.6%) declined (30 non-IT and five IT centres) mainly as they did not have eligible patients and, in a minority of cases, due to local bureaucratic/logistic issues. The remaining 37 centres declared interest to participate to the study and availability to submit the protocol to their local IRB. Notably, among all the contacted centres, 25 are certified as CoE by ENETS. At the time of this analysis, 14 of 37 (37.8%) centres were active to enrol and 8 of 37 (21.6%) were actively recruiting (2/6 IT and 6/8 non-IT centres). Data from 89 patients were entered. The median age was 57 (22–87) years at the time of NEN diagnosis and 64 (24–92) years at the time of COVID-19 diagnosis. The main characteristics of NENs are reported in Table 1. Most patients had a gastroenteropancreatic (GEP) primary site, well-differentiated tumour, metastatic stage and non-functioning status. At the time of testing positive

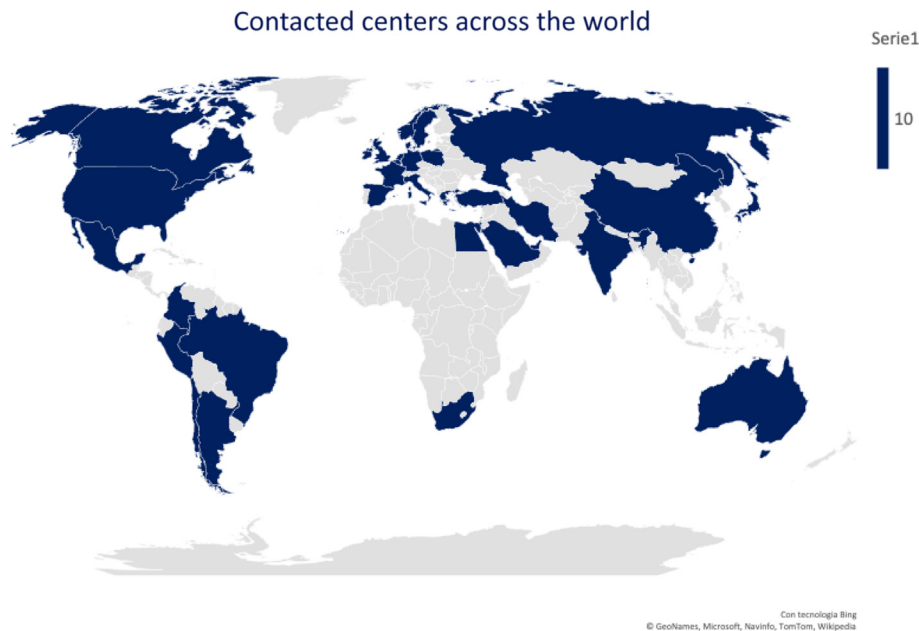


Fig. 1. Contacted centres across the world. This figure reports in blue all the centres across the world contacted for the survey.

for COVID-19, half of them were receiving treatment with long-acting SSA, a minority in combination with other therapies, 11.7% RLT, mainly with lutetium¹⁷⁷-DOTATATE, and only 12% of the total were receiving chemotherapy.

Sixty-two patients (72.9%) had comorbidities, most commonly arterial hypertension (46.7%), diabetes mellitus (33.8%) or both (17.7%).

The main characteristics of COVID-19 are reported in Table 2. The most frequent symptoms/signs were fever and cough, whereas 11 patients were asymptomatic and one third had pneumonia. Regarding COVID-19 treatment, three patients needed sub-intensive care, whereas no patient needed ICU. Antibiotics were the most common medical therapy. In most patients, no change of the anti-tumour therapy occurred. The use of anti-COVID-19 therapy was variable, with one patient receiving sub-intensive care and three patients a combination of oxygen therapy, anticoagulant, antibiotics and glucocorticoids. Seven patients (6 GEP neuroendocrine tumours [NETs] and 1 GEP neuroendocrine carcinoma [NEC]) died due to COVID-19. Four patients were on SSA, one on everolimus (EVE), one on RLT and one on combination treatment with cabozantinib and atezolizumab, within clinical trials. Moreover, three were diagnosed with pneumonia and six were hospitalised before the fatal event. Finally, two had diabetes mellitus and arterial hypertension, one diabetes mellitus, arterial hypertension and chronic renal failure, one diabetes mellitus alone and one arterial hypertension and prostatic benign hypertrophy. The remaining two had no comorbidities.

Lastly, we performed the analyses for correlations of COVID-19–related mortality and age, sex and NEN primary site. Mortality related to the age was: 20–49: 0/

Table 1

Main characteristics of neuroendocrine neoplasms.

Total N of patients	89
Sex	N (%)
Male	59 (66.3)
Female	30 (33.7)
Age range	N (%)
20–49	27 (30.3)
50–75	54 (60.7)
>75	8 (9.0)
Type of NEN	
• GEP NET	67 (75.2)
• GEP NEC	3 (3.3)
• Thoracic NET	10 (11.2)
• Thoracic NEC	2 (2.2)
• Other NET	4 (4.5)
• Other NEC	3 (3.3)
Tumour stage	
• Metastatic	76 (85.3)
• Locally advanced	13 (14.6)
Site of distant metastasis	
• Liver alone	22 (24.7)
• Liver + extrahepatic	43 (48.3)
• Extrahepatic alone	11 (12.3)
Functional status	
• Functioning	16 (17.9)
• Non-functioning	73 (82.0)
Anti-tumour treatment	
• None	18 (20.2)
• SSA	45 (50.5)
• Chemo	11 (12.3)
• RLT	10 (11.2)
• EVE	4 (4.5)
• TKI	5 (5.6)
• Other	8 (8.9)

NEN, neuroendocrine neoplasm; GEP, gastroenteropancreatic; NET, neuroendocrine tumour; NEC, neuroendocrine carcinoma; SSA, somatostatin analogue; RLT, radioligand therapy; EVE, everolimus; TKI, tyrosine kinase inhibitor.

Table 2
COVID-19 features.

Total N. of patients	89
Age range	N (%)
20–49	18 (20.2)
50–75	56 (62.9)
>75	15 (16.9)
Symptoms/signs	
• Asymptomatic	11 (12.3)
• Fever	57 (64.0)
• Cough	45 (50.5)
• Asthenia	22 (24.7)
• Exertional dyspnoea	20 (22.4)
• Rest dyspnoea	17 (19.0)
• Anosmia/dysgeusia	15 (16.8)
• Pneumonia	30 (33.7)
• No features	58 (65.1)
Treatment	
• Intensive care unit	0 (–)
• Sub-intensive	3 (3.3)
• O ₂	14 (15.7)
• Antibiotics	26 (29.2)
• Steroids	16 (17.9)
• Hydroxychloroquine	8 (8.9)
• Anticoagulant	6 (6.7)
• Antiviral	7 (7.8)
Anti-tumour therapy	
• No change	64 (71.9)
• Temporary interruption	22 (24.7)
• Discontinuation	3 (3.3)
COVID-19 clinical outcome	
• Death	7 (7.8)
• Complete recovery	74 (83.1)
• Sequelae	8 (8.9)

COVID-19, coronavirus disease 2019.

18 (0%); age 50–75: 5/56 (9%); age >75: 2/15 (13%) ($p = 0.15$). For what concerns sex, all the 7 of patients were men. Lastly, the mortality related to the tumour primary site was given as follows: GEP 7/70 (10%); thoracic 0/11 (0%); other 0/8 (0%) ($p = 0.79$).

4. Discussion

In this study, we described the demographic and clinical features of patients with NEN along with a confirmed positive nasopharyngeal swab RT-PCR test for SARS-CoV-2. The characteristics of the enrolled patients with NENs seem to reflect those of the NEN general population, regardless of COVID-19, including mainly low-/intermediate-grade, metastatic, non-functioning GEP NEN, on treatment with therapies targeting somatostatin receptor-2 expressed in the great majority of well-differentiated NENs. Our analysis did not suggest relationships between SARS-CoV-2 infection/disease/mortality and specific features of NENs. Although sporadic NEN cases were reported in general COVID-19 registries of patients with cancer [23], this is the first study specifically focused on patients with NENs positive for SARS-CoV-2.

Even when different types of cancers were correlated with COVID-19 mortality, NEN cases were not reported [16]. In one of the largest investigations of SARS-CoV-2 in patients with cancer which was first focused specifically on patients receiving anti-tumour treatment, among around 60,000 patients with cancer analysed, no NENs were reported [35].

Our series represents the result of a worldwide data collection among centres dealing with patients with NENs. Most patients had a well-differentiated GEP NET reflecting the real-world NEN scenario. This could be surprising if we consider that GEP NETs are usually slow growing and not treated with chemotherapy. Moreover, therapies such as EVE or RLT, which are often used in patients with NENs, may produce immunosuppression and lymphopenia, both considered to favour COVID-19 infection.

The 7.8% of mortality observed in our study is much lower than the 33% reported for lung cancer with the thoracic cancers international covid 19 collaboration (TERAVOLT) study [23], reflecting the different populations studied and the seemingly increased risk of death among patients with lung cancer and COVID-19 [23]. Comparison across studies of patients with cancer and COVID-19 is challenging given the heterogeneity of the populations studied and variations in therapy provided, including access to antiviral therapy and intensive care. Haematological and pulmonary malignancies have been reported to be associated with a higher mortality rate from COVID-19 compared with other types of cancer [14,15,36,37], although others did not observe a similar effect [12]. On the other hand, patients with different types of cancer have been reported to have variable SARS-CoV-2 susceptibility and COVID-19 disease phenotypes, with notable increased SARS-CoV-2 susceptibility in patients with haematological cancers [16].

Platinum and etoposide regimen is a chemotherapy usually administered to patients with NECs. In our study, eight patients with NECs were included and two of them were on platinum-etoposide. A recent publication of probably the largest series of patients with cancer and COVID-19 reported that platinum-etoposide was one of the risk factors correlated with higher COVID-19 mortality rate [38]. Other studies have similarly reported worse outcomes in patients receiving cytotoxic chemotherapy [39,40], but not all studies support that recent chemotherapy administration is associated with higher risk of death [12,41].

Our study has several limitations. First, the selection of the participant centres was arbitrary, and it is unclear if they were the right context to check patients with NENs and SARS-CoV-2. They were primarily larger academic ones with substantial expertise in managing patients with NENs and potentially with more resources to handle critically ill patients with COVID-19. Nevertheless, it is possible that they may not accurately reflect the care provided to patients with NENs and COVID-19

in the community or, more simply, that COVID-19 was managed at non-NEN-referral centres, and therefore, our analysis could have missed a proportion of them. It is probable that most patients suffering from NENs are managed by NEN-referral institutions. Second, although more than 80 patients are a relatively high number, considering the rarity of NENs, it is still relatively low in absolute, given the high prevalence of patients with NENs in the community at any given time, and the probability that COVID-19 occurred in patients with NENs frequently, especially in high-risk areas. Third, our survey was more focused on the NEN rather than the COVID-19 context, as it mainly regarded NEN-referral centres. Therefore, although it was quite spread across the world, we cannot be sure that these data are representative of the topic as it is not clear whether it is more probable to capture this information in the COVID-19 context or in the NEN context. Some knowledge about NEN coming from the COVID-19 context could be reported soon with the CCC-19 and/or ESMO Co-Care surveys. Last, although the contacted centres were representative of all five continents, this analysis reported data about six European, one USA and one Middle East centres. Notably, areas such as India, Brazil, UK, Russia and Mexico that were highly impacted in terms of COVID-19 mortality declared not to have specific information about NEN cases. Similarly, it is notable that Chinese centres (the Guangzhou and Wuhan centres and the Chinese Study group for NET, CSNET, were contacted) did not have any patients with NENs and COVID-19 although they managed a very high number of NEN cases. Unfortunately, other highly affected areas, such as Chile (Pontifical Catholic University of Chile) and Brazil (Camargo Cancer Center, Sao Paulo), did not join the survey due to logistic/bureaucratic issues. A further limitation of our study is the lack of information about the actual incidence of COVID-19 in this population.

However, the major strength of this study is being the only one to date that specifically focused on COVID-19 and NEN and involved many NEN centres worldwide. Furthermore, the high response rate to the survey (88.8%) is promising in terms of worldwide representation.

5. Conclusion

Although the specific incidence, morbidity and mortality related to COVID-19 among patients with NENs remain to be defined, our analysis is the first to specifically capture data about morbidity and mortality in a similar population. However, most patients with NEN and COVID-19 infection present with a relatively mild illness, although mortality was increased over what it is seen in the population of patients with COVID-19 without cancer. Despite its inherent limitations, it provides helpful insight indications on clinical management

of patients with NENs during the COVID-19 pandemic, in compliance with the rules of general protection but also by applying anticancer therapy and appropriate supportive care.

Author contribution

N.F. contributed to conceptualisation and writing the original draft. V.B. contributed to methodology and formal analysis. L.G. and F.S. contributed to the collection and extraction of data. N.F., L.G., T.R.H., A.L.S., J. Hofland, J. Hernando, M.B.S., R.G.-C., J.C., W.W.d.H., G.K., M.R., S.G.-G., K.O., A.L., M.R., and F.S. contributed to investigation and resources. D.T. and S.B. contributed to data curation and software. N.F., L.G., T.R.H., A.L.S., J. Hofland, J. Hernando, M.B.S., R.G.-C., J.C., W.W.d.H., G.K., M.R., S.G.-G., K.O., A.L., M.R., and F.S. contributed to reviewing, editing and approving the final manuscript.

Conflict of interest statement

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 article.

Acknowledgements

The authors thank all the patients and their families. The authors thank all the researchers involved in this study. This research did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

References

- [1] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395(10223): 507–13.
- [2] Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;382(8): 727–33.
- [3] Woolf SH, Chapman DA, Sabo RT, Zimmerman EB. Excess deaths from COVID-19 and other causes in the US, march 1, 2020, to january 2, 2021. *JAMA* 2021 Apr 2;325(17):1786–9.
- [4] Al-Shamsi HO, Alhazzani W, Alhuraiji A, et al. A practical approach to the management of cancer patients during the novel coronavirus disease 2019 (COVID-19) pandemic: an international collaborative group. *Oncologist* 2020 Jun;25(6):e936–45.
- [5] Yu J, Ouyang W, Chua MLK, Xie C. SARS-CoV-2 transmission in patients with cancer at a tertiary care hospital in Wuhan, China. *JAMA Oncol* 2020 Jul 1;6(7):1108–10.
- [6] Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020; 21(3):335–7.
- [7] Lunski MJ, Burton J, Tawagi K, et al. Multivariate mortality analyses in COVID-19: comparing patients with cancer

- and patients without cancer in Louisiana. *Cancer* 2021;127(2):266–74.
- [8] Wang Q, Berger NA, Xu R. Analyses of risk, racial disparity, and outcomes among US patients with cancer and COVID-19 infection. *JAMA Oncol* 2021;7(2):220–7.
- [9] Venkatesulu BP, Chandrasekar VT, Girdhar P, et al. A systematic review and meta-analysis of cancer patients affected by a novel coronavirus. *JNCI Cancer Spectr* 2021;5(2). pkaa102.
- [10] Zhang H, Han H, He T, et al. Clinical characteristics and outcomes of COVID-19-infected cancer patients: a systematic review and meta-analysis. *J Natl Cancer Inst* 2021;113(4):371–80.
- [11] Giannakoulis VG, Papoutsis E, Siempos II. Effect of cancer on clinical outcomes of patients with COVID-19: a meta-analysis of patient data. *JCO Glob Oncol* 2020;6:799–808.
- [12] Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020;395(10241):1907–18.
- [13] Saini KS, Tagliamento M, Lambertini M, et al. Mortality in patients with cancer and coronavirus disease 2019: a systematic review and pooled analysis of 52 studies. *Eur J Canc* 2020;139:43–50.
- [14] de Jooode K, Dumoulin DW, Tol J, et al. Dutch Oncology COVID-19 consortium: outcome of COVID-19 in patients with cancer in a nationwide cohort study. *Eur J Canc* 2020;141:171–84.
- [15] Jee J, Foote MB, Lumish M, et al. Chemotherapy and COVID-19 outcomes in patients with cancer. *JCO* 2020 Oct 20;38(30):3538–46. <https://www.ncbi.nlm.nih.gov/pubmed/32795225>. Updated Oct 20. Accessed 30, 38.
- [16] Lee LYW, Cazier JB, Starkey T, et al. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. *Lancet Oncol* 2020;21(10):1309–16.
- [17] Weickert MO, Robbins T, Kyrou I, et al. Impact of the COVID-19 pandemic on neuroendocrine tumour services in England. *Endocrine* 2021;71(1):14–9.
- [18] Krug S, Garbe J, Konig S, et al. Professional assessment of the impact of COVID-19 on handling NET patients. *J Clin Med* 2020;9(11).
- [19] Bergsland EK, Halperin DM, Dillon JS, et al. North American neuroendocrine tumor society guide for neuroendocrine tumor patient health care providers during COVID-19. *Pancreas* 2020;49(6):723–8.
- [20] Rodriguez-Freixinos V, Capdevila J, Pavel M, et al. Practical recommendations for the management of patients with gastroenteropancreatic and thoracic (carcinoid) neuroendocrine neoplasms in the COVID-19 era. *Eur J Canc* 2021;144:200–14.
- [21] Bodei L, Bergsland E, de Herder WW, et al. Peptide receptor radionuclide therapy during the COVID-19 pandemic: are there any concerns? *J Nucl Med* 2020;61(8):1094–5.
- [22] Casey RT, Valk GD, Schalin-Jantti C, Grossman AB, Thakker RV. Endocrinology in the time OF COVID-19: clinical management of neuroendocrine neoplasms (NENs). *Eur J Endocrinol* 2020;183(2):G79–88.
- [23] Garassino MC, Whisenant JG, Huang LC, et al. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. *Lancet Oncol* 2020;21(7):914–22.
- [24] Ramirez RA, Bren-Mattison Y, Thiagarajan R, et al. A neuroendocrine tumor specialty center in new orleans' (NOLANETS) response to patient care during the COVID-19 pandemic. *Oncologist* 2020;25(7):548–51.
- [25] Gu WT, Zhou F, Xie WQ, et al. A potential impact of SARS-CoV-2 on pituitary glands and pituitary neuroendocrine tumors. *Endocrine* 2021 May;72(2):340–8.
- [26] Mindaye ET, Kassahun M, Tigiy G. Bronchial carcinoid tumor in the era of covid-19 pandemic: a case report. *Int J Surg Case Rep* 2021;80:105703.
- [27] Krishnapriya V, Rathore P, Kumar S, et al. COVID-19-Positive report posing a delay in treatment course in a middle-aged metastatic neuroendocrine tumor patient. *Indian J Palliat Care* 2020;26(Suppl 1):S173–5.
- [28] Tzeng CD, Tran Cao HS, Roland CL, et al. Surgical decision-making and prioritization for cancer patients at the onset of the COVID-19 pandemic: a multidisciplinary approach. *Surg Oncol* 2020;34:182–5.
- [29] Koukouraki S, Kapsoritakis N, Bourogianni O. COVID-19 pandemic: implications for radionuclide therapy in Nuclear Medicine departments. *Hellenic J Nucl Med* 2020;23(Suppl):31–4.
- [30] Panzuto F, Maccauro M, Campana D, et al. Impact of the SARS-CoV2 pandemic dissemination on the management of neuroendocrine neoplasia in Italy: a report from the Italian Association for Neuroendocrine Tumors (Itanet). *J Endocrinol Invest* 2021 May;44(5):989–94.
- [31] Spada F, Pellicori S, Zampino G, et al. SARS-CoV-2-related pneumonia can be successfully managed in patients with metastatic neuroendocrine tumors: a critical point of view. *Endocrine* 2020;70(1):6–10.
- [32] Riechelmann RP, Peixoto RD, Fernandes GDS, et al. Evidence-based recommendations for gastrointestinal cancers during the COVID-19 pandemic by the Brazilian Gastrointestinal Tumours Group. *Ecancermedicallscience* 2020;14:1048.
- [33] Paganelli G, Bodei L, Modlin I. A metastatic tumor is no different to a viral pandemic: lessons learnt from COVID-19 may teach us to change the PRRT paradigm. *Eur J Nucl Med Mol Imag* 2020;47(10):2223–6.
- [34] <https://www.who.int>. Accessed.
- [35] Aschele C, Negru ME, Pastorino A, et al. Incidence of SARS-CoV-2 infection among patients undergoing active antitumor treatment in Italy. *JAMA Oncol* 2021;7(2):304–6.
- [36] Dai M, Liu D, Liu M, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. *Canc Discov* 2020;10(6):783–91.
- [37] Mehta V, Goel S, Kabarriti R, et al. Case fatality rate of cancer patients with COVID-19 in a New York hospital system. *Canc Discov* 2020;10(7):935–41.
- [38] Grivas P, Khaki AR, Wise-Draper TM, et al. Association of clinical factors and recent anti-cancer therapy with COVID-19 severity among patients with cancer: a report from the COVID-19 and cancer consortium. *Ann Oncol* 2021 Jun;32(6):787–800.
- [39] Lievre A, Turpin A, Ray-Coquard I, et al. Risk factors for Coronavirus Disease 2019 (COVID-19) severity and mortality among solid cancer patients and impact of the disease on anti-cancer treatment: a French nationwide cohort study (GCO-002 CACOVID-19). *Eur J Canc* 2020;141:62–81.
- [40] Yekeduz E, Utkan G, Urun Y. A systematic review and meta-analysis: the effect of active cancer treatment on severity of COVID-19. *Eur J Canc* 2020;141:92–104.
- [41] Lee LY, Cazier JB, Angelis V, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet* 2020;395(10241):1919–26.