


COVID-19 in Patients with Cancer: A Retrospective Study of 212 Cases from a French SARS-CoV-2 Cluster During the First Wave of the COVID-19 Pandemic

SOPHIE MARTIN,^a CHARLOTTE KAEUFFER,^b PIERRE LEYENDECKER,^c NICOLAS TUZIN,^d YOUSSEF TAZI,^f FRÉDÉRIQUE SCHAFF-WENDLING,^g TIFFANIE KLEINHENY,^h STÉPHANIE HUSSON-WETZEL,ⁱ GUILLAUME PAMART,^e JEAN-MARC LIMACHER,^j OLIVIER CLERC,^k ELISE DICOP,^a JEAN-EMMANUEL KURTZ,^a PHILIPPE BARTHÉLÉMY,^a JUSTINE GANTZER ^a

^aDepartment of Medical Oncology, ICANS, Strasbourg, France; Departments of ^bInfectious Diseases, ^cRadiology, ^dPublic Health, and ^eChest Diseases, Strasbourg, University Hospital, Nouvel Hôpital Civil, Strasbourg, France; ^fDepartment of Medical Oncology, Clinique Sainte-Anne, Strasbourg, France; ^gDepartment of Medical Oncology, Clinique de l'Orangerie, Strasbourg, France; Departments of ^hMedical Oncology and ⁱGastroenterology, Groupe Hospitalier de la région Mulhouse Sud Alsace, Mulhouse, France; ^jDepartment of Medical Oncology and Clinical Hematology, Hôpital Louis Pasteur, Colmar, France; ^kRehabilitation Center, Maison de Santé Béthel, Oberhausbergen, France

Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Cancer • COVID-19 • Retrospective cohort • Mortality • Risk factor • Patient management

ABSTRACT

We describe a large series of patients with solid tumors in an early COVID-19 cluster in the eastern part of France. From February to May 2020, this multicenter retrospective study enrolled 212 patients with cancer under treatment or on follow-up for any type of malignant solid tumor and positive for SARS-CoV-2. The mortality rate was 30%. Patients with gastrointestinal cancers were

identified as a subset of more vulnerable patients; immunotherapy and radiotherapy within 3 months from COVID-19 diagnosis were risk factors for death. The reported data support the essential need to be proactive and weigh the risks of morbidity from COVID-19 against the magnitude of benefits of intended cancer therapies during this pandemic. *The Oncologist* 2021;26:e1656–e1659

Implications for Practice: This article supports the essential need to be proactive (treatment delay or modification) in oncology in the setting of pandemic. This study identified patients with gastrointestinal cancers as a more vulnerable subset of patients with cancer and found that immunotherapy and radiotherapy within 3 months from COVID-19 diagnosis to be risk factors for death. The reported data indicate the necessity of weighing the risks of morbidity from COVID-19 against the magnitude of benefits of intended cancer therapies in any future wave of COVID-19.

INTRODUCTION

In December 2019, China was affected by SARS-CoV-2, which rapidly spread to a pandemic. Alsace became an epidemic cluster of the COVID-19 outbreak while France was only at the first stage of the epidemic. Despite the first national lockdown established between March 16 and May 11, 2020, the first epidemic wave in France caused a total of 26,785 deaths [1]. Patients with cancer were considered to be a vulnerable population because of their disease and treatments [2, 3], alongside all patients with comorbidities [4, 5].

The primary objective of this study was to determine the mortality rate due to COVID-19 in patients with cancer.

Analyses of prognostic factors, treatment modification, and the consequences of oncologists' attitudes in terms of cancer treatment in the setting of the pandemic were secondary objectives.

RESULTS

Description of Patients

Between February 20 and May 7, 2020, 212 patients were enrolled from departments of medical oncology, pneumology, and gastroenterology in Strasbourg University Hospital

Correspondence: Justine Gantzer, M.D., Department of Medical Oncology, ICANS, 17 rue Albert Calmette, BP 23025, 67033 Strasbourg, France. Telephone: 33-68-76-66-66; e-mail: j.gantzer@icans.eu Received July 22, 2020; accepted for publication May 11, 2021; published Online First on June 3, 2021. <http://dx.doi.org/10.1002/onco.13831>

No part of this article may be reproduced, stored, or transmitted in any form or for any means without the prior permission in writing from the copyright holder. For information on purchasing reprints contact commercialreprints@wiley.com. For permission information contact permissions@wiley.com.

Table 1. Tumor characteristics at baseline

Tumor characteristics	All patients (n = 212), n (%)	Patients who died (n = 63), n (%)	Patients who survived (n = 149), n (%)
Tumor type			
Breast	45 (21)	6 (10)	39 (26)
Gastrointestinal	50 (24)	22 (35)	28 (19)
Colon	24 (11)	10 (16)	14 (9)
Pancreas	8 (4)	1 (2)	7 (5)
Esophagus	7 (4)	3 (5)	4 (3)
Stomach	6 (3)	4 (6)	2 (1)
Liver	5 (2)	4 (6)	1 (1)
Lung	32 (15)	10 (16)	22 (15)
Genitourinary cancer	37 (17)	11 (17)	26 (17)
Prostate	18 (8)	2 (3)	16 (11)
Kidney	9 (4)	5 (8)	4 (3)
Bladder	8 (4)	4 (6)	4 (3)
Testicle	2	0	2
Other	48 (23)	14 (22)	34 (23)
Gynecological	12 (6)	5 (8)	7 (5)
Sarcoma	12 (6)	4 (6)	8 (5)
Head and neck	10 (5)	0	10 (7)
Skin	7 (4)	3 (5)	4 (3)
Central nervous system cancers	5 (2)	1	4 (3)
Thymoma	1	0	1
Unknown primary	1	1	0
Cancer stage			
Localized	70 (33)	15 (24)	55 (37)
Metastatic	142 (67)	48 (76)	94 (63)
Metastatic sites			
Pleuropulmonary metastases	58 (27)	24 (38)	34 (23)
Other sites of metastases	84 (40)	24 (38)	60 (40)
Treatment setting			
Adjuvant/neoadjuvant	38 (18)	4 (6)	34 (23)
First line metastatic	62 (29)	17 (27)	45 (30)
Second line or later metastatic	63 (30)	22 (35)	41(28)
Palliative care	17 (8)	11 (18)	6 (4)
Remission	32 (15)	9 (14)	23 (15)
Cancer treatment within 3 months from COVID-19			
Chemotherapy	99 (47)	26 (41)	73 (49)
Immunotherapy	8 (4)	6 (10)	2 (1)
Targeted therapy	22 (10)	4 (6)	18 (12)
Hormonotherapy	16 (8)	3 (5)	13 (9)
Radiotherapy	47 (22)	20 (32)	27 (18)
Surgery	30 (14)	9 (14)	21 (14)
None	42 (20)	11 (17)	31 (21)
Influence of treatment decisions			
Treatment modification (group 1)	56 (26)	6 (10)	50 (33)
No treatment modification (group 2)	74 (35)	24 (38)	50 (33)
No systemic treatment ongoing (group 3)	82 (39)	33 (52)	49 (33)

Table 2. Multivariate analysis and odds ratio for death

Variables	Odds ratio [95% CI]	p value
Patient characteristic		
Performance status 1	1	
Performance status 2	1.97 [0.71–5.42]	.1832
Performance status 3–4	6.76 [2.84–17.24]	.0001
No prior malignancy	1	
Prior malignancy	2.47 [1.04–5.93]	.0398
Treatment within 3 months from COVID-19 diagnosis		
No systemic treatment	1	
Chemotherapy	0.51 [0.16–1.53]	.2342
Immunotherapy	11.03 [1.26–137.87]	.0405
Targeted therapy	0.46 [0.07–2.32]	.3648
Hormonotherapy	0.30 [0.03–1.98]	.2378
No radiotherapy	1	
Radiotherapy	3.29 [1.32–8.41]	.0108
Cancer type		
Breast	1	
Lung	1.07 [0.25–4.60]	.9177
Genitourinary tract	2.71 [0.68–11.74]	.1633
Gastrointestinal	6.02 [1.81–22.65]	.0049
Other sites of cancer	1.42 [0.41–5.24]	.5826
Influence of treatment decisions		
No systemic treatment ongoing (group 3)	1	
Treatment modification (group 1)	0.19 [0.05–0.66]	.011
No treatment modification (group 2)	1.76 [0.57–5.53]	.32

Abbreviation: CI, confidence interval.

($n = 54$), the Strasbourg Cancer Institute ($n = 61$), two clinics ($n = 45$), the general hospitals in Colmar ($n = 11$) and Mulhouse ($n = 32$), and one rehabilitation center ($n = 9$). The median age was 67 years. Sex ratio was 1:1. Among the 212 enrolled patients, 172 (81%) had comorbidities (smoking, hypertension, thrombotic cardio-cerebrovascular disease, chronic obstructive pulmonary disease, or lung surgery). A medical history of previous malignancy (either solid tumor or hematologic) unrelated to the current disease was found in 46 patients (22%). Cancer types and treatment are detailed in Table 1.

To evaluate oncologists' attitudes in terms of cancer treatment during this period, we identified three groups of patients. Group 1 included patients with all actions taken prior to confirmation of COVID-19: (a) treatment delayed in patients with mild symptoms compatible with COVID-19 or recent COVID-19 contact; (b) treatment delayed at patient's request; or (c) treatment modification, neoadjuvant chemotherapy interrupted to move on surgery, or steroid discontinuation. Group 2 included patients with (a) no treatment modification (asymptomatic patients or treatment considered to be urgent) or (b) any anticancer treatment in the

10 days prior to COVID-19 diagnosis or death. Group 3 included patients without ongoing systemic treatment.

COVID-19 Diagnosis

The first patient included with highly suggestive clinical signs of COVID-19 had his symptoms on February 20, before which date no case was reported in the Alsace area. SARS-CoV-2 infection diagnosis was documented by positive real-time reverse transcriptase polymerase chain reaction ($n = 141$), serological tests ($n = 17$), and chest computed tomography (CT) scan ($n = 113$). Moreover, 23 COVID-19 radiological diagnoses were obtained during CT scan performed for radiotherapy or tumor assessments. We enrolled 17 patients because of a combination of symptoms, a prior contact, and a compatible chest x-ray.

Patients' Care and Outcomes

Among the 212 patients, 64 (30%) did not require hospital admission, whereas 148 (70%) were hospitalized, including 25 (12%) in intensive care units.

The mortality rate in the study population was 30% ($n = 63$).

Of the 149 patients who survived, 36 (24%) reported loss of autonomy or malnutrition, and 15 (10%) required oxygen therapy at home. Seventy-eight of 106 eligible patients received post-COVID-19 systemic anticancer treatment. Twelve did not receive subsequent anticancer therapy but did receive best supportive care because of disease progression or worsening of general condition (partly due to COVID-19).

Prognostic Factors

Fifteen significant variables were retained to perform the multivariate analysis (Table 2): age, gender, performance status, smoking, chronic obstructive pulmonary disease or lung surgery, prior malignancy, narcotic prescription, cancer type, stage history of systemic treatment or radiotherapy, active versus controlled disease, and whether anticancer treatment was modified or delayed before COVID-19.

Patients with a poor performance status were at significantly higher risk of death. A prior history of unrelated malignancy was strongly associated with the risk of death from COVID-19 as opposed to other comorbidities. Patients with gastrointestinal cancer were at higher risk of death as compared with other localizations. Patients on therapy within the 3 months from COVID-19 diagnosis were not at higher risk of death if they had chemotherapy as opposed to radiotherapy. The use of immune checkpoint inhibitors was also associated with a higher risk of death. Finally, patients from group 1 (treatment modification) were at lower risk of death.

DISCUSSION

Our data, reporting a 30% overall mortality rate, need to be considered in the light of the fact that our area had an early cluster when COVID-19 guidelines for patients with cancer were not yet available [6].

We found that being proactive for patients with suspected COVID-19 significantly reduced the risk of death,

as opposed to stopping cancer therapy after the diagnosis of COVID-19, which appeared to be too late.

However, the reduction in COVID-19 mortality during cancer treatment is only part of the task, as cancer mortality could increase in the months and years to come because of delays in diagnosis or treatment during the pandemic [7, 8]. Moreover, it will be interesting to assess whether the changes in treatment during the first wave, although clearly beneficial at the time, will have negative effects in the long term with an evolution of the oncological disease [9].

There is also some uncertainty to the consequences of COVID-19 in subsets of patients (especially immunotherapy) where cooperative efforts are warranted to build large cohorts.

The best way to be able to conduct oncology treatment as desired is to prevent the risk of COVID-19. Today, vaccination can be offered to all patients with cancer, regardless of their type of treatment, because no interaction between the different vaccines and anticancer treatments has been described [10].

CONCLUSION

Our data show that patients with cancer are exposed to a higher risk of COVID-19 mortality. Our experience in one of

the first COVID-19 clusters highlights that learning from the oncology community to adapt cancer care has been and is a key for patients with cancer in the context of this pandemic.

ACKNOWLEDGMENTS

We thank all patients and physicians involved in the study with a particular emphasis on intensive care unit colleagues and health care staff who agreed to participate in this project despite the current health crisis. The authors are also indebted to Drs. Christine Essner, H el ene Joosen, Magali Edel, France Campos, Meher Ben Abdelghani, Laure Pierard, Micka el Burgy, Christian Borel, Lucile Pabst, Carole Pflumio, Philippe Trenszy, Emilie Hutt, and Laure De Cock as well as Prof. Georges No el, Yves Hansmann, Samira Fafi-Kremer, and Micka el Ohana for their help and fruitful discussions on this work.

DISCLOSURES

The authors indicated no financial relationships.

REFERENCES

1. Informations coronavirus. French government Web site. <https://www.gouvernement.fr/info-coronavirus>.
2. 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. *Cancer Discov* 2020;10:783–791.
3. Wu Z, McGoogan JM. 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* 2020; 323:1239–1242.
4. Wang D, Hu B, Hu C et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020;323:1061–1069.
5. Zhang L, Zhu F, Xie L et al. Clinical characteristics of COVID-19-infected cancer patients: A retrospective case study in three hospitals within Wuhan, China. *Ann Oncol* 2020;31: 894–901.
6. Cancers solides et COVID-19: les recommandations du Haut Conseil de la Sant e Publique. Accessed March 19, 2020.
7. Sud A, Jones ME, Broglio J et al. Collateral damage: The impact on outcomes from cancer surgery of the COVID-19 pandemic. *Ann Oncol* 2020;31:1065–1074.
8. H equet D, Rodrigues M, Tardivon A et al. Impact de l' pid mie de COVID-19 sur les demandes de prise en charge initiale pour cancer du sein. *Bull Cancer* 2020;107:620–622.
9. European Society for Medical Oncology Web site. <https://www.esmo.org>.
10. Institut National du Cancer Web site. <https://www.e-cancer.fr>.