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admissions, and meeting composite severe illness endpoints.¹

The findings raised concern for an increased risk of overall mortality in patients with cancer (13%). We believe that the uncertainties in the study¹ make the results difficult to interpret in subgroups of patients, particularly in patients with haematological malignancies.

928 patients met the inclusion criteria and 204 (22%) of the patients had haematological malignancies; however, the number of patients in each of the subtypes of haematological malignancies in total was 305 patients, not 204, and these patients were subdivided as follows: 102 with lymphoid neoplasms, 55 with multiple myeloma, 54 with low-grade non-Hodgkin lymphoma, 42 with myeloid neoplasms, 27 with high-grade non-Hodgkin lymphoma, 13 with acute myeloid leukaemia, six with acute lymphoblastic leukaemia, and six with unspecified cancers. These numbers mean that 101 cases of various haematological malignancies were unexplained. This discrepancy between the total reported number of patients with haematological malignancies (n=204) and the total number of patients reported in the subtypes (n=305) could be explained by the fact that several patients might have been in multiple subcategories.

Haematological malignancies might be associated with differential risks of infection and complications secondary to COVID-19, since myeloid and lymphoid neoplasms affect the immune systems differently; therefore, this factor should be evaluated in detail. The authors only mentioned patients who had multiple cancer types (n=107), solid tumours (n=654), and haematological malignancies alone (n=167) as they assessed for secondary and primary outcomes, with no additional details regarding the combination of cancers. For example, patients might have had a history of haematological neoplasms currently in remission (off chemotherapy)

with another active solid cancer, or vice versa, which would have made a substantial difference in the treatment strategy and degree of immunodeficiency, thus resulting in the risk of severe COVID-19. In particular, patients with leukaemia are often immunosuppressed with possible hypogammaglobulinaemia, leading to further severe clinical outcomes associated with COVID-19. Furthermore, the authors did not follow the revised 2016 WHO classification when detailing the haematological malignancies.²

45% of the analysed population had a cancer status labelled as having remission with no evidence of disease.¹ However, no details were given regarding what types of malignancy were in remission. It is crucial to know the relative rates of remission between patients with solid tumours and haematological malignancies, and whether they were on maintenance therapy.

Finally, although the types of anticancer therapy used were described, the objective parameters for measuring the severity of resulting immunosuppression, such as white blood cell counts, absolute neutrophil counts, or absolute lymphocyte counts, were not. Additionally, it would have been informative to know the concentrations of inflammatory cytokine markers (eg, interleukin-6) in the patients reviewed. Ruan and colleagues³ showed that lower absolute lymphocyte counts and increases in interleukin-6 concentrations were linked to a poor outcome in patients with COVID-19. Of interest, several studies calculated the ratios of neutrophils to lymphocytes and of lymphocytes to C-reactive protein to show systemic inflammation and predict more severe clinical outcomes in patients infected with COVID-19.⁴

The severity of COVID-19 infections in patients with cancer is an important clinical question. The analysis¹ would have benefited from enhanced subset disease evaluation, including more

specific types of cancer, markers of immune status and inflammation, and type of treatment regimen.

We declare no competing interests.

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Authors' reply

We thank Dimitrios Moris and colleagues and Alexandre Malek and colleagues for their insightful commentary about the CCC19 study findings.¹ We value the opportunity to further characterise mortality outcomes beyond our initial report.¹

With a median of 30 days (IQR 21–90) follow-up, as of Aug 21, 2020, 30-day all-cause mortality increased to 20% (154 of 754 patients who either died within 30 days or had at least 30 days of follow-up). Planned time-to-event analyses will refine these estimates. 121 (79%) deaths were attributed to respiratory failure (appendix). In our cohort,¹ the category of respiratory failure encompasses deaths from any respiratory failure syndrome. Although respiratory failure caused by cancer, its therapies, or other comorbidities could confound the cause of death attribution, this is unavoidable. Diagnostic procedures are challenging with COVID-19, autopsies are rare, and Vital Statistics Reporting Guidance specifically directs medical certifiers to



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list COVID-19 as the underlying cause of death, with the most immediate cause of death (eg, respiratory failure) listed first.² Because this method might overestimate COVID-19-related deaths, we reported all-cause mortality.

We share Moris and colleagues' concerns regarding the potential increase of cancer mortality caused by delays in cancer screening, diagnosis, and care delivery because of severe acute respiratory syndrome coronavirus 2—a concern already borne out in some early analyses.³ The prospect of widening existing racial and socioeconomic disparities in cancer outcomes is of real concern and central to forthcoming analyses of our cohort.

Malek and colleagues discuss important limitations in applying the results to patients with haematological malignancies. The small number of patients with specific haematological malignancies in the CCC19 cohort required the broad categorisation with non-exclusive categories, resulting in apparent numerical discrepancies. Only 53 (26%) patients with haematological malignancies were in remission, limiting the conclusions in this subgroup (appendix). Subsequent studies have shown a high risk of severe COVID-19 outcomes for patients with haematological malignancies.^{4,5} Despite a larger sample size, these analyses still do not have the power to identify, at the granular level, associations between the clinical status of the haematological malignancy, therapeutic modalities, and outcomes. The CCC19 cohort now includes more than 900 patients with haematological malignancies, and further analyses are underway.

Regarding laboratory data, 449 (48%) patients presented with mild COVID-19, most of whom had no available baseline laboratory data. Additionally, our sample size only allowed the interrogation of the reported clinical variables (which were established a priori) in multivariable modelling. We agree that examining the independent prognostic value of laboratory parameters is vital; we will soon present a larger analysis

addressing this. Although we firmly support robust methods and highlight limitations, it is imperative to deliver timely and valuable information to the community.

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Lockdown impact on COVID-19 epidemics in regions across metropolitan France

Lockdowns have been used by most European countries in response to the COVID-19 pandemic. In France, a national lockdown was implemented on March 17, 2020. Some have questioned the need for a nationwide implementation given that most hospital admissions were concentrated in two of 13 regions; others have even questioned the impact of the lockdown on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread, arguing that the natural epidemic peak was about to be reached. Here we discuss the impact of lockdown on COVID-19 epidemics in regions across metropolitan France.

On March 17, 2020, daily hospital admissions were indeed highest in Grand-Est (5.3 per 100 000 inhabitants) and Île-de-France (3.6 per 100 000 inhabitants) regions. Yet a surge in COVID-19 hospital admissions was occurring at that time across all regions of metropolitan France, as depicted in the appendix. The COVID-19 epidemic spread from the eastern to the western parts of France, crossing the daily hospitalisation threshold of 1 per 100 000 inhabitants between March 10 (Grand-Est) and March 23, 2020 (Bretagne and Nouvelle-Aquitaine). Île-de-France (Paris region) experienced the highest rate of hospital admissions per day (10.0 per 100 000 inhabitants), and Bretagne the lowest (1.3 per 100 000 inhabitants). Regardless of the time the epidemic started in the region, and its scale, 12 of 13 regions experienced a peak in daily hospital admissions on average 11 days (range 8–14 days) after the lockdown was implemented. This figure corresponds to the mean duration between infection and hospital admission for the patients experiencing severe forms of disease.¹ Since the different

See Online for appendix