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Letter to the Editor

High mortality of cancer patients in times of SARS-CoV-2: Do not generalize!



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To the Editor of the *European Journal of Cancer*,

Being heavily involved in the treatment of patients with cancer in times of the SARS-CoV-2 pandemic [1,2], we read with great interest the articles of Assaad *et al.* [3] and Yarz *et al.* [4] in the *European Journal of Cancer*. Assaad *et al.* [3] performed an exciting retrospective analysis of 302 patients with presenting between March 1st and April 15th 2020 in the Comprehensive Cancer Center of Lyon with a suspicion of Corona Virus disease (COVID) -19 [3]. In 55 (18.2%) of them the Cobas real-time polymerase chain reaction (PCR, Roche, Neuilly) was positive for SARS-CoV-2 and in 247 (81.8%), it proved to be negative. Computed tomography scanning of the chest was suspect for COVID-19 in respectively 27 (67.5%) and 59 (29.5%) of both groups. Thirty patients (9.9%) died during the observation period, the majority (24/30, 80%) with metastatic disease. Surprisingly

mortality was not statistically different in the PCR-positive compared with the PCR-negative patients: 8 of 55 (14.5%) versus 22 of 247 (8.9%) at 25 days, respectively. Although the authors are right to state that COVID-19 is underdiagnosed with current diagnostic test methods, it is at least misleading to claim that patients with cancer presenting with a cough, fever, muscle pain, diarrhoea, muscle pain, anosmia or neurological problems have unrecognised COVID-19. These complaints were also common in the pre-SARS-CoV-2 era and can be caused by (advanced) cancer, cancer treatment and other medication, concomitant comorbidity, non-SARS-CoV-2 infections or allergic reactions. Particularly, infectious morbidity is expected to be more frequent in autumn, when seasonal common colds, flues and bacterial infections will become more prevalent in patient populations and will likely cause diagnostic problems. Repetitive SARS-CoV-2 PCR testing is, at this moment, the only way to minimise false-negative test results. Currently, there are no generally accepted criteria to make a diagnosis of COVID-19 based on clinical symptoms only, although they can sometimes be highly suspicious. This is an important issue as in times limited of resources, the label ‘cancer with COVID-19’ can compromise the access of intensive care unit (ICU) and outcome of patients dramatically in overwhelmed

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healthcare systems due to the outbreak of the SARS-CoV-2 pandemic. This was illustrated by the Thoracic Cancers International COVID-19 Collaboration, a multicenter observational registry on clinical data of 200 patients with PCR-confirmed COVID-19 and thoracic cancers, diagnosed between March 26 and April 2020. One hundred fifty-two (76%) patients were hospitalised and 66 (33%) died. Strikingly only 13 (10%) of 134 patients who met criteria for ICU admission were admitted to the ICU [5]. Prioritising ICU admission implicated that many of these patients did not receive optimal ICU care. It also happened in Belgium, although the limits of mechanical ventilation support and ICU bed capacity were far from reached, but beds were kept free ‘for future patients with a better long-term prognosis’. May this, besides the limited statistical power of the study explain (some of) the results of the Assaad *et al.* [3] article?

It is of paramount importance that cancer patients should not be stigmatised to be too vulnerable to start or continue treatments of proven value, propending for delays or no treatment at all [1]. Therefore, one should be careful to reiterate and generalize in the literature that ‘patients with cancer have a high mortality rate’. The present data suggest that particularly patients with ongoing treatment for active locally advanced and metastatic solid cancers and haematological malignancies have a poorer outcome and higher mortality after a SARS-CoV-2 infection, but this seems not to be the case for other cancer settings [1,5,7]. In the article by Yarza *et al.* [4], 82% of the patients had metastatic disease, and mortality was particularly high in this group compared with the non-metastatic patients but not significantly different, again probably due to small numbers (respectively 29% versus 9%). The OpenSAFELY study, looking at factors associated with 5683 COVID-19-related hospital deaths in the linked electronic health records of 17 million adult National Health Service (NHS) patients, clearly showed that male gender (hazard ratio [HR] = 1.99; 95% confidence interval [CI] = 1.80–2.10), age (with a very strong gradient), ethnicity (adjusted HR = 1.71; 95% CI = 1.44–2.02), uncontrolled diabetes (HR = 2.26 95% CI = 2.18–2.56), obesity (with a very strong gradient) and various other medical conditions often had a higher impact on the probability to die of SARS-CoV-2 than cancer [6]. This was confirmed in the study of Robilotti *et al.* [7] on the experiences of 423 cases of symptomatic COVID-19 in Memorial Sloan Kettering Cancer Center from 10 March to 7 April 2020. Risk factors should all be taken into account in a balanced way making decisions for active treatment and ICU admission of patients with COVID-19 if resources are limited, not discriminating patients with cancer per se as many of them have an excellent prognosis. The rapidly expanding literature on COVID-19 should be interpreted with caution as it is often hampered by

methodological and statistical flaws [1]. Many articles have a limited sample size, biased patient selection criteria, a retrospective design and several entangled cofactors involved which were often not corrected for. In addition, the hospitalised patients with cancer during the peak of the COVID-19 epidemic in general are at the worse end of the spectrum, having end-stage metastatic disease, complications of surgery or systemic treatment or other comorbidities requiring treatment, which make them more prone for fatal complications. Conclusions drawn from these patient groups should not be generalised for all patients with cancer. Several adaptations in cancer care organisation by means of protective measures, social distancing, minimising the number of hospital attendances, aggressive testing for SARS-CoV-2 in patients and healthcare providers, telemonitoring, artificial intelligence and better knowledge of risk factors for severe morbidity proved to be helpful to provide cancer care safely in the majority of patients in times of SARS-CoV-2 with a good outcome [1,2,5,7]. This letter is a plea for selection of patients with cancer on an individual basis to give them maximal access to (adapted) treatment and if necessary maximal supportive care in times of the SARS-CoV-2 pandemic.

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