Reply to COVID-19 in Patients With Hematological Malignancies: Considering the Role of Tyrosine Kinase Inhibitors

We thank Morales-Ortega and his colleagues for their interest in our study[1] and particularly in patients with chronic myeloid leukemia (CML).

In our study,[1] we evaluated the incidence of coronavirus disease 2019 (COVID-19) in March 2020 according to hematological diagnosis in the Brescia cohort, and we observed that COVID-19 was contracted by none of the patients affected by CML in the Brescia cohort and by 2 patients in the Milan cohort. A low incidence of COVID-19 in patients with CML has been described in other studies.[2,3] Notably, the actual incidence in our cohort may have been underestimated because, during March 2020, only patients with severe symptoms were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Italy, as discussed in our article. Nevertheless, patients with CML were less represented in our series of symptomatic hematological patients with COVID-19. In addition to the effect of imatinib on virus entry, we agree that the immunomodulatory effects cited by Morales-Ortega and other authors[4] may mitigate acute lung injury and reduce the frequency of symptomatic disease.

The mortality rate reported in our study was 50% for patients with CML/myeloproliferative neoplasms and COVID-19, and both patients with COVID-19 and CML were reported to have died. The very low number of patients did not allow any general conclusion to be drawn about mortality rates; the confidence limits of the proportion ranged from less than 20% to more than 80%. In fact, both patients with CML who died had unusual clinical characteristics in comparison with the average patient with CML. Both were old (73 and 77 years, respectively) and had numerous comorbidities (heart failure secondary to ischemic cardiopathy, metastatic colon adenocarcinoma, and chronic renal failure in one and Parkinson disease, methicillin-resistant *Staphylococcus aureus* infection of a hip prosthesis, depressive syndrome, and chronic renal and heart failure in the other). Moreover, both were receiving reduced doses of tyrosine kinase inhibitors and had lost their molecular response at the time of death as a result of frequent interruptions of imatinib treatment. Advanced hematological disease and comorbidities have been associated with unfavorable outcomes for patients with COVID-19 and CML,[3] and advanced age is often reported as a risk factor for mortality in the general COVID-19 population.[5]

In conclusion, the role of tyrosine kinase inhibitors as protective factors against SARS-CoV-2 infection in patients with CML should be confirmed by large-scale epidemiologic studies, but their biological and therapeutic role merits further investigation in ongoing studies (NCT04346147, NCT04357613, NCT04394416, and NCT04422678).

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