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

In an article previously published in *Cancer*, Cattaneo et al[1] analyzed a cohort of patients with coronavirus disease 2019 (COVID-19) and hematological malignancies in March 2020, and they highlighted that subjects with chronic myeloid leukemia (CML) had a lower than expected frequency of COVID-19. The authors linked this observation to the lower level of immunodeficiency seen in CML and to a potential protective role of tyrosine kinase inhibitors (TKIs) based on the possible antiviral activity of these drugs. However, they reported a mortality rate 30 days after the documentation of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection of 50% in the group of patients with chronic myeloproliferative malignancies, which included patients with CML (78% of these patients were treated with TKIs).

As the authors insightfully pointed out in their article, imatinib (the main TKI for CML treatment) has shown antiviral effects against other betacoronaviruses in in vitro studies, probably by preventing virus entry into host cells via interference with the fusion between viral and cellular membranes.[2,3] Regarding SARS-CoV-2, there are conflicting data about the antiviral potential of this drug: although significant suppression of viral replication in Vero E6 cells has been described,[4] no potent effect over the virus lifecycle in Caco-2 cell cultures has been recently reported with the standard dosage of imatinib (400-800 mg/d).[5]

Furthermore, imatinib might exert its potential protective role in COVID-19 through its immunomodulatory properties.[6] Murine models of sepsis and acute lung injury have suggested that this drug has a beneficial effect by reducing pulmonary edema, preventing histological damage, and improving endothelial barrier integrity, probably by attenuating the release of proinflammatory cytokines, including interleukin 6 and tumor necrosis factor α.[7,8] This cytokine downregulation has also been observed in patients with CML[9] and seems to be mediated by the inhibition of transcription factor NF-κB according to previous evidence from animal and human cell studies.[10] This is particularly interesting because the NF-κB pathway has been pointed out as one of the main inflammatory signaling cascades leading to the pulmonary damage observed in severe COVID-19.[11] In this regard, both a lower incidence and a lower severity of this condition have been consistently reported in subjects with CML.[12-14] In fact, Passamonti et al[15] have recently found that all patients with CML under TKI treatment in their Italian multicenter cohort of hematological patients with a SARS-CoV-2 infection were alive at the end of follow-up.

In conclusion, we consider that the positive outcomes of TKI-treated CML patients with COVID-19, including a lower frequency of SARS-CoV-2 infection and a higher survival rate, strengthen the hypothesis that these drugs might be beneficial in the treatment of this disease. Hence, we believe that a more detailed description by Cattaneo et al[1] about deceased subjects with CML under TKI therapy in their study would be valuable. Finally, further clinical research should be encouraged to assess the effectiveness of imatinib and other related TKIs in COVID-19.

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CONFLICT OF INTEREST DISCLOSURES

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