



Chronic myelogenous leukemia

Chronic myeloid leukemia management at the time of the COVID-19 pandemic in Italy. A campus CML survey

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It has been reported that imatinib may have a specific protective role in blocking the fusion of the protein S of the Coronavirus belonging to the viral surface with cell membranes [1]. This role could prevent the endocytosis necessary for the viral activation of different viral species (Sars-COV, MERS-CoV, and IBV) [2]. No in vivo information has been reported so far. The only information related to chronic

myeloid leukemia (CML) comes from a relatively small series from the Hubei Province where it was found that relatively few COVID-19+ CML patients were reported [3].

The Campus CML is an ongoing program aimed at creating a network of physicians in Italy involved in different aspects of the management of patients with CML, sharing experiences and updates for the diagnosis, treatment of the disease, identification and prevention of the specific toxicity of the drugs used but also on possible future therapeutic approaches. Considering the current COVID-19 emergency in Italy, we asked Italian clinicians about the incidence of infections among their CML patients and about the management of the disease in this unique pandemic period. On April 6 we sent an ad hoc questionnaire to 51 Campus CML centers throughout the country and 47 centers (92%) have completed the online survey. Nineteen centers were from the most affected regions: Lombardia, Piemonte, Veneto, Emilia-Romagna. Twelve centers (42.5%) reported a decrease in the incidence of new CML cases in this period. Data from a large cohort of 6883 CML patients were gathered: only 12 cases of confirmed COVID-19 infection were reported (0.17%) up to the middle of April. Two of the 12 cases were healthcare professionals and 8 have been infected in the most affected Italian regions. Only two deaths have been recorded, one in a patient aged 91 years. Other five patients were suspected based on the symptoms presented, but tested negative. The majority of participants (89%) declared that CML patients were tested only in case of fever and/or related symptoms and/or who had been in close contact with a positive subject, but not routinely. In Italy, testing is routinely performed on inpatients. Eight centers (17%) reported difficulties in performing a baseline diagnostic work-up and molecular monitoring to detect MRD during treatment. Sixty-six percent of centers postponed the molecular analysis by 1–2 months during this emergency if

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patients were at least in MR3 or if they were in deep and stable molecular response. Patients who did not have to perform a molecular monitoring were checked prevalently by telephone or by email during the COVID-19 pandemic. The COVID-19 emergency had a repercussion on the treatment-free remission (TFR) strategy: 58% of participating physicians did not propose a possible discontinuation and 24% of patients already in TFR have had to modify the molecular monthly monitoring approach. We recorded changes also in the delivery of drugs: while imatinib delivery was not affected due to local pharmacy distributions, 36% of physicians reported consequences for second-generation TKIs subject to AIFA (the Italian Medicine Agency) monitoring in Italy. In some instances, delivery was carried out directly at the patient's home (12%) or a supply for more months has been granted (10%) by the treating center.

The activity of ongoing CML trials has already been affected by the emergency: 34% of physicians have stopped enrollment and 8% have continued with the ongoing trials with some difficulties in the planned follow-up of enrolled patients. AIFA issued a decree that allowed patients enrolled in a trial and not able to reach the center to perform the requested tests at a hospital near home with a complete reimbursement: 51% of interviewed centers adopted this strategy.

These results of our survey show that the incidence of COVID-19 infection has so far proven extremely low in CML patients treated with TKIs. These data are in line with what observed in adult patients with Ph+ acute lymphoblastic leukemia (Ph+ ALL) in Italy, where patients are induced with a TKI plus steroids and no systemic chemotherapy, and could continue to be managed even at the peak of the COVID-19 outbreak [4]. Taken together, the data gathered on over 7000 cases of CML and Ph+ ALL support a potential role of TKIs in protecting patients from COVID-19 infection. To conclusively answer this question a randomized study (EudraCT 2020-001236-10) is verifying the effect of imatinib in preventing pulmonary vascular leak in patients with severe COVID-19 disease. Although the likelihood of developing a symptomatic COVID-19 infection in CML patients in Italy is close to zero and lower than that of the general population in Italy, the current pandemic emergency is, however, already negatively impacting on different aspects of the day-to-day management of patients, on disease monitoring and on treatment decisions, as well as on the enrollment in and compliance to clinical trials.

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