The recent spread of the coronavirus disease 2019 (COVID-19) infection has raised important questions within the haematology community on how best to manage and treat patients with haematological malignancies, particularly acute leukaemias. Italy has witnessed a dramatic rise in infections and death rates, which has affected, in particular, certain

Philadelphia-positive acute lymphoblastic leukaemia (ALL) in Italy during the COVID-19 pandemic: a Campus ALL study

© 2020 British Society for Haematology and John Wiley & Sons Ltd
British Journal of Haematology, 2020, 190, e1–e38
areas of the most populated northern regions of the country (Lombardia, Veneto, Piemonte, Emilia Romagna). Within the nationwide Campus Acute Lymphoblastic Leukaemia (ALL) programme, in the last week of March, we sent a questionnaire addressing different issues related to the management of adult patients with ALL during the COVID-19 pandemic to 40 haematology centres located across the country. Twenty-four centres were based in Northern Italy (i.e. north of Rome), which has been most affected by the COVID-19 outbreak. So far, in the large majority of centres throughout the country, patients are screened prior to being admitted as inpatients, while this procedure is not routinely carried out in most centres for outpatients, unless they present with symptoms potentially ascribable to the COVID-19 infection. In the present analysis, we focussed on Philadelphia-positive (Ph+) ALL, for which a second questionnaire was sent at the beginning of April. The interest in Ph+ ALL relates to its incidence, which increases with age accounting for approximately 50% of B-lineage ALL patients aged >50 years, to the key role played by tyrosine kinase inhibitors (TKIs) and to the approach taken in Italy to treat adult Ph+ ALL. We obtained information on 267 adult patients with Ph+ ALL treated in induction with a TKI plus steroids, with no TKI-based treatment. In addition, a chemotherapy-free consolidation approach, in our case with blinatumomab, can further reduce the post-remission hospitalisation.

The possibility that TKIs may play a role in protecting patients from the COVID-19 infection has been suggested pre-clinically and a randomised study aimed at verifying the effect of imatinib in preventing pulmonary vascular leak in patients with severe COVID-19 is ongoing (EudraCT 2020-001236-10). Finally, an immunosuppressed status may not be a risk factor for COVID-19 adverse events, as documented also in patients with liver transplants. It becomes increasingly important that patients with Ph+ ALL are rapidly identified at diagnosis and we once again advocate for a chemotherapy-free induction strategy. It is worth recalling that with dasatinib (and steroids) alone, 20–25% of patients can become molecularly negative and that with the addition of blinatumomab this increases to 60%. Under such a TKI-based strategy in Italy, adult Ph+ ALL of all ages could continue to be managed as before even during the outbreak and peak of the COVID-19 epidemic.

Acknowledgements

The authors wish to thank all the Campus ALL colleagues who provided data of their patients. Partly supported by Associazione Italiana Ricerca sul Cancro (AIRC), Special 5 × 1000 Program Metastases (21198), Milan (Italy) to RF.

Robin Foà1
Massimiliano Bonifacio2
Sabina Chiaretti1
Antonio Curti3
Anna Candoni4
Carmen Fava5
Maria Ciccone6

© 2020 British Society for Haematology and John Wiley & Sons Ltd
British Journal of Haematology, 2020, 190, e1–e38
SARS-CoV-2 infection anxieties and general population restrictions delay diagnosis and treatment of acute haematological malignancies

Acute leukaemias remain a very serious group of diseases often associated with major complications and substantial morbidity and mortality. Diagnosis and appropriate anti-leukaemic therapy together with any needed supportive therapy should be started as soon as possible. Any delay in diagnosis or treatment increases the probability of additional medical complications, including hyperleukocytosis with related leukostasis, tumour lysis syndrome and coagulopathies or myeloid extramedullary masses. In addition, patients with acute leukaemias are highly susceptible to infectious diseases unrelated to the disease itself, to treatment side effects and to individual risk factors.

• Severe infectious diseases, such as the plague, cholera and yellow fever, have been the cause of pandemics throughout recorded human history including in the past two centuries. For example, 14 international conferences were held between 1851 and 1938 to coordinate responses to major infectious outbreaks. Restrictive measures including quarantine and social distancing measures were established and guidelines for sanitary management of contagious disease were developed. These conferences aimed to maximize protection from disease with minimum effects on trade and travel.

From its emergence in China, SARS-CoV-2 virus has spread all around the world, representing the most serious health, economic and social crisis of the new millennium. Since the beginning of the SARS-CoV-2 epidemic in Italy, the Italian Government has implemented several restrictive measures to contain the spread of infection. Among these measures, the lockdown implemented on 9 March 2020 has a positive impact on disease propagation, in particular in the central and southern regions of Italy. Unfortunately, the

References

1. Chiaretti S, Vitale A, Cazzaniga G, Orlando SM, Silvestri D, Fazi P, et al. Clinico-biological features of 5202 patients with acute lymphoblastic leukemia enrolled in the Italian AIEOP and GIMEMA protocols and stratified in age cohorts. Haematologica. 2013;98:1702–10.
2. Chiaretti S, Foà R. Management of adult Ph-positive acute lymphoblastic leukemia. Hematol Am Soc Hematol Educ Program. 2015;2015:406–13.
3. Vignetti M, Fazi P, Cimino G, Martinelli G, Di Raimondo F, Ferrara, F, et al. Imatinib plus steroids induces complete remissions and prolonged survival in elderly Philadelphia chromosome-positive patients with acute lymphoblastic leukemia without additional chemotherapy: results of the Gruppo Italiano Malattie Ematologiche dell’Adulto (GIMEMA) LAL0201-B protocol. Blood. 2007;109:3676–8.
4. Foà R, Vitale A, Vignetti M, Meloni G, Guarini A, De Propris, M, et al. Dasatinib as first-line treatment for adult patients with Philadelphia chromosome-positive acute lymphoblastic leukemia. Blood. 2011;118:6521–8.
5. Chiaretti S, Bassan R, Vitale A, Elia L, Picicci A, Puzzolo, C, et al. Dasatinib-blinatumomab combination for the front-line treatment of adult Ph+ ALL patients. Updated results of the GIMEMA LAL2116 D-Alba trial. Blood. 2019;134:740.
6. Nguyen DD, Gao K, Chen J, Wang R, Wei GW. Potentially highly potent drugs for 2019-nCoV. bioRxiv. 2020 [Epub ahead of print]. DOI: https://doi.org/10.1101/2020.02.05.936013.
7. Sarzi-Puttini P, Giorgi V, Sirotti S, Marotto D, Ardizzone S, Rizzardini, G, et al. COVID-19, cytokines and immunosuppression: what can we learn from severe acute respiratory syndrome? Clin Exp Rheumatol. 2020;38:357–42.
8. Ferro F, Elefante E, Baldini C, Bartolani E, Puxeddu I, Talarico, R, et al. COVID-19: the new challenge for rheumatologists. Clin Exp Rheumatol. 2020;38:175–80.
9. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson, JJ et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020;395:1033–4.
10. D’Antiga L. Coronaviruses and immunosuppressed patients. The facts during the third epidemic. Liver Transpl. 2020 [Epub ahead of print]. https://doi.org/10.1002/lt.25756.