bjh research paper

COVID-19 infection in chronic myeloid leukaemia after one year of the pandemic in Italy. A Campus CML report

Massimo Breccia,[1] Elisabetta Abruzzese,[2] Vincenzo Accurso,[3] Immacolata Attolico,[4] Sara Barulli,[5] Micaela Bergamaschi,[6] Gianni Binotto,[7] Monica Bocchia,[8] Massimiliano Bonifacio,[9] Giovanni Caocci,[10] Isabella Capodanno,[11] Fausto Castagnetti,[12] Francesco Cavazzini,[13] Elena Crisà,[14] Monica Crugnola,[15] Maria Stella De Candia,[16] Chiara Elena,[17] Carmen Fava,[18] Sara Galimberti,[19] Antonella Gozzini,[20] Gabriele Gugliotta,[12] Tamara Intermesoli,[21] Alessandra Iurlo,[22] Gaetano La Barba,[23] Roberto Latagliata,[24] Sabrina Leonetti Crescenzi,[25] Luciano Levato,[26] Giuseppina Loglisci,[27] Alessandro Lucchesi,[28] Luigiana Luciano,[29] Francesca Lunghi,[30] Debora Luzi,[31] Alessandra Malato,[32] Maria Cristina Miggiano,[33] Michele Pizzuti,[34] Patrizia Pregno,[35] Davide Rapezzi,[36] Giovanna Rege-Cambrin,[37] Gianantonio Rosti,[28] Sabina Russo,[38] Rosaria Sancetta,[39] Anna Rita Scortechini,[40] Federica Sorà,[41] Paolo Sportoletti,[42] Fabio Stagno,[43] Agostino Tafuri,[44] Mario Tiribelli,[45] Robin Foà[1,*] and Giuseppe Saglio[46,*]

[1]*Department of Translational and Precision Medicine, Sapienza University,* [2]*Sant Eugenio Hospital, Hematology, Roma,* [3]*UO di Ematologia con Trapianto, AU Policlinico Paolo Giaccone, Palermo,* [4]*UO Ematologia con Trapianto, Università degli Studi di Bari Aldo Moro, Bari,* [5]*Divisione di Ematologia di Muraglia, CTMO Ospedale San Salvatore, Pesaro,* [6]*Ematologia, Ospedale Santa Corona,*

Summary

Limited information is available on the impact of the COVID-19 pandemic on the management of chronic myeloid leukaemia (CML). The Campus CML network collected retrospective information on 8 665 CML patients followed at 46 centres throughout Italy during the pandemic between February 2020 and January 2021. Within this cohort, we recorded 217 SARS-CoV-2-positive patients (2·5%). Most patients (57%) were diagnosed as having SARS-CoV-2 infection during the second peak of the pandemic (September 2020 to January 2021). The majority (35%) was aged between 50 and 65 years with a male prevalence (73%). Fifty-six percent of patients presented concomitant comorbidities. The median time from CML diagnosis to SARS-CoV-2 infection was six years (three months to 18 years). Twenty-one patients (9·6%) required hospitalization without the need of respiratory assistance, 18 (8·2%) were hospitalized for respiratory assistance, 8 (3·6%) were admitted to an intensive care unit, while 170 (78%) were only quarantined. Twenty-three percent of patients discontinued tyrosine kinase inhibitor (TKI) therapy during the infection. Twelve patients died due to COVID-19 with a mortality rate of 5·5% in the positive cohort and of 0·13% in the whole cohort. We could also document sequelae caused by the SARS-CoV-2 infection and an impact of the pandemic on the overall management of CML patients.

Keywords: chronic myeloid leukemia, Covid-19, prognosis, mortality.

First published online 11 October 2021
doi: 10.1111/bjh.17890

Pietra Ligure, [7]Ematologia ed Immunologia Clinica, Università degli Studi di Padova, Padova, [8]U.O.C. Ematologia e Trapianti, A.O. Senese – Policlinico 'Le Scotte', Siena, [9]Divisione di Ematologia, Istituti Ospitalieri di Verona, Policlinico G.B. Rossi, Verona, [10]CTMO – Ematologia, Ospedale 'Businco', Cagliari, [11]Ematologia, Azienda Unità Sanitaria Locale-IRCCS, Reggio Emilia, [12]Istituto di Ematologia 'Lorenzo e A. Seragnoli', Policlinico S. Orsola-Malpighi, Bologna, [13]Ematologia, Arcispedale Sant'Anna, Ferrara, [14]S.C.D.U. Ematologia – DIMECS e Dipartimento Oncologico, Università del Piemonte Orientale Amedeo Avogadro, Novara, [15]Ematologia, Università degli Studi di Parma, Parma, [16]UOC Ematologia con Trapianto, Brindisi Hospital, Brindisi, [17]Ematologia, Fondazione IRCCS Policlinico S. Matteo, Pavia, [18]A.S.O. Ordine Mauriziano, P.O. Umberto I, Struttura Complessa a Direzione Universitaria-Ematologia e Terapie Cellulari, Torino, [19]Ematologia, Università di Pisa – Azienda Ospedaliera Pisana, Pisa, [20]Unità di Ricerca e di Malattie del Sangue, Ematologia San Luca Vecchio, Firenze, [21]Hematology, Bergamo Hospital, Bergamo, [22]UOC Ematologia, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, [23]U.O. Ematologia Clinica, Azienda USL di Pescara, Pescara, [24]Ematologia, Ospedale Belcolle, Viterbo, [25]Ematologia, Ospedale S. Giovanni Addolorata, Roma, [26]Ematologia, Ospedale Catanzaro, Catanzaro, [27]Ematologia, Ospedale Lecce, Lecce, [28]Ematologia, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) 'Dino Amadori', Meldola, [29]Ematologia, Azienda Ospedaliera Universitaria – Università degli Studi di Napoli 'Federico II', Napoli, [30]Ematologia, Ospedale S. Raffaele, Milano, [31]Ematologia, A.O. Santa Maria – Terni S.C Oncoematologia, Terni, [32]Ematologia, Ospedali Riuniti 'Villa Sofia-Cervello', Palermo, [33]Ematologia, Ospedale Vicenza, Vicenza, [34]Ematologia, Ospedale Potenza, Potenza, [35]Dipartimento di Oncologia ed Ematologia S.C. Ematologia 2, A.O. Città della Salute e della Scienza di Torino S. G. Battista, Torino, [36]Ematologia, Ospedale

Cuneo, Cuneo, [37]*Dipartimento di Scienze Cliniche e Biologiche, Ospedale S. Luigi Gonzaga-Medicina Interna 2, Orbassano,* [38]*Dipartimento di Medicina Interna, Azienda Ospedaliera Universitaria – Policlinico G. Martino, Messina,* [39]*Ematologia, Ospedale Mestre, Mestre,* [40]*Ematologia, Azienda Ospedaliero – Universitaria Ospedali Riuniti, Ancona,* [41]*Ematologia, Policlinico Gemelli – Università Cattolica del Sacro Cuore, Roma,* [42]*Ematologia, Ospedale Perugia, Perugia,* [43]*Hematology Section and BMT Unit, AOU Policlinico 'Rodolico-San Marco', Catania,* [44]*Ematologia, AOU S. Andrea, Roma,* [45]*Clinica Ematologica-Centro Trapianti e Terapie cellulari, Azienda Ospedaliero-Universitaria, Udine, and* [46]*A.S.O. Ordine Mauriziano, Struttura Complessa a Direzione Universitaria-Ematologia e Terapie Cellulari-, P.O. Umberto I, Torino, Italy*

Received 11 July 2021; accepted for publication 27 September 2021
Correspondence: Massimo Breccia, Hematology, Department of Translational and Precision Medicine, Sapienza University, Via Benevento 6, Rome 00161, Italy.
E-mail: breccia@bce.uniroma1.it

*Robin Foà and Giuseppe Saglio contributed equally.

Introduction

An outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) started in December 2019 in the province of Hubei in China and then became pandemic in March 2020. Italy was one of the first and most affected countries, and the first lockdown was declared on 9 March 2020. Several reports have been published on the prevalence of the SARS-CoV-2 infection among patients with haematologic malignancies.[1,2] Limited information is available regarding chronic myeloid leukaemia (CML) patients. A relatively small series of CML patients was reported from the Hubei Province: an increased rate of infections was described compared to the general population with five patients defined as positive and 17 suspected for the onset of respiratory symptoms but not confirmed by nasal swab.[3] During phase 1 of the pandemic, the Campus CML group carried out a survey in Italy on the management of CML during the first lockdown and in a series of 6 883 CML patients reported a COVID-19 incidence of 0·17%, with only 12 positive patients.[4] Then, the Dutch group showed that only one out of 148 patients recorded in CMyLife, a nationwide web-based portal, tested positive.[5] Sixteen CML patients with SARS-CoV-2 infection were reported by the Turkish group and compared to 48 controls.[6] A lower rate of intensive care unit (ICU) admissions and mechanical ventilation were reported with a shorter period of hospitalization and a lower rate of mortality in CML patients: 6·3% compared to 12·8% in the control group. The results of the first Campus CML survey[4] referred to a short period from February to the end of April 2020, the peak of the first pandemic wave in Italy. We thereafter conducted a second survey that covered the period between May 2020 and August 2020, and a final survey that covered the period up to January 2021 in order to evaluate the temporal course of the infection and the characteristics of COVID-19-positive CML patients during one year of the pandemic in Italy.

Patients and methods

The Campus CML nationwide programme was launched in January 2019 and has enabled collecting information by over

50 haematology centres throughout Italy. Campus CML aims to take stock of the state of the art in the field of 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. During phase 1 of the pandemic (February–April 2020), after a call conference with the coordinators of the different working groups, a first questionnaire addressing issues about CML management during the pandemic and incidence of the infection in the clinical practice was prepared. We then launched a second and third survey during the pandemic phases 2 and 3, i.e. May-August 2020 and September 2020–January 2021, which allowed collecting in an aggregate manner the baseline characteristics of CML patients who experienced the infection, incidence, grading of the infection and rate of mortality, without exclusion criteria. Considering the nature of the research, based on a questionnaire with aggregated data, no approval from the ethics committee was required. The impact of SARS-CoV-2 infection on the management of the disease was also documented.

Results

Incidence and baseline characteristics of COVID-19-positive CML patients

We obtained retrospective information on 8 665 CML patients followed and managed at 46 centres throughout the country. Within this cohort, we recorded 217 SARS-CoV-2-positive patients at the molecular level, with an incidence of 2·5% (Table I). Analysing the results reported in the three different periods, most patients (57%) were diagnosed as having SARS-CoV-2 infection between September 2020 and the end of January 2021 (phase 3 of the pandemic), whereas 30% were diagnosed during phase 1 (February–April 2020) and only 13% in phase 2 between May and August 2020 (Fig 1). A male prevalence was observed (73%). Most of the SARS-CoV-2-positive patients were aged between 50 and 65 years (39%), with 27% being younger than 50, 20% between 65 and 75, and 14% being over 75 years old. The median time from CML diagnosis to SARS-CoV-2 infection was six years (range three months to 18 years). Fifty-six percent of patients presented concomitant comorbidities at the time of infection, the most frequent being arterial hypertension (34%), followed by diabetes (22%), dyslipidaemia (15%), other cardiovascular diseases (11%) and a concomitant neoplasia (2%).

At COVID-19 diagnosis, 27% of patients were receiving imatinib, 26% nilotinib, 18% dasatinib, 8% ponatinib, 8% bosutinib, 2% asciminib, while 11% were not on treatment after a successful treatment-free remission (TFR; Table I). At the time of infection, 85% of patients were in molecular response ranging between MR3 [ratio *BCR/ABL1* ≤0·1% International Scale (IS)] and deep MR (MR4, ratio *BCR/ABL1* ≤0·01% IS, and MR4.5, ratio *BCR/ABL1* ≤0·0032% IS),[7] 6% were in complete cytogenetic remission, 3% in partial cytogenetic remission and 6% in complete haematological response. Thus, 15% of patients were not in molecular response at the time of the infection.

Table I. Baseline characteristics of COVID-19-positive CML patients.

	Total 217 patients
Gender	
Male	73%
Female	27%
Age	
<50	27%
50–65	39%
65–75	20%
>75	14%
Concomitant comorbidities	
Hypertension	34%
Diabetes	22%
Dyslipidaemia	15%
CV disorders	11%
Neoplasia	2%
No comorbidities	44%
Type of drug	
Imatinib	27%
Nilotinib	26%
Dasatinib	18%
Bosutinib	8%
Ponatinib	8%
Asciminib	2%
TFR	11%
Type of response	
Molecular response (MR3–MR4.5)	85%
Complete cytogenetic response	6%
Partial cytogenetic response	3%
Complete haematologic response	6%

CML, chronic myeloid leukaemia; CV, cardiovascular; TFR, treatment-free remission.

SARS-CoV-2 infection severity, outcome and sequelae

At the time of COVID-19 diagnosis, similar to the normal population not affected by CML, 28% of patients presented fever and respiratory symptoms, 13% cough, 10% isolated fever, 13% ageusia, 12% anosmia, 4% had more than one symptom, while 20% were completely asymptomatic (Fig 2). Twenty-one patients [World Health Organization (WHO) mild form, 9·6%] required hospitalization without the need of respiratory assistance, 18 (WHO moderate form, 8·2%) were hospitalized for respiratory assistance, eight (WHO severe and critical forms, 3·6%) were admitted to an ICU, while 170 patients (78%) were only quarantined (Table II). Twenty-three percent of patients discontinued TKI therapy during the infection due to hospitalization. In 49% of patients the source of the contagion was familiar, in 18% it was due to work, in 3% it occurred in healthcare

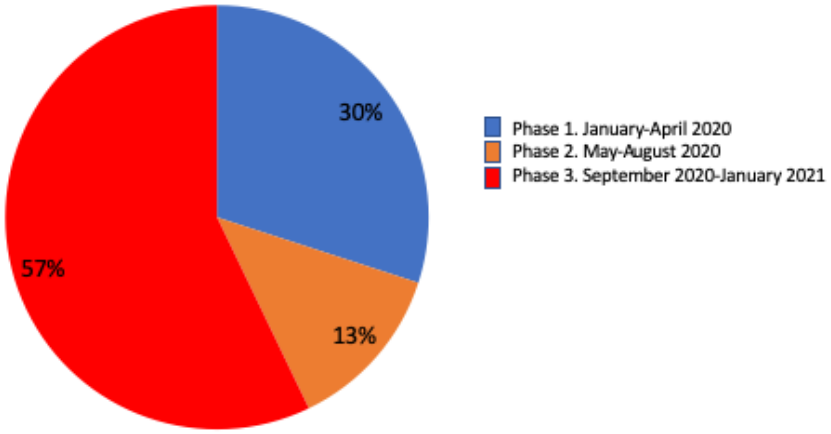

Fig 1. Covid-19 incidence according to the phase of the pandemic. [Colour figure can be viewed at wileyonlinelibrary.com]

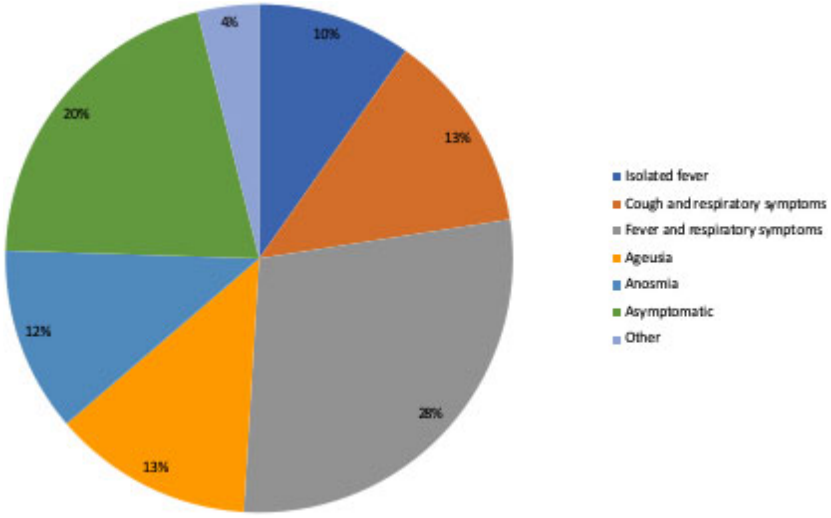

Fig 2. Presenting symptoms at the time of COVID-19 diagnosis. [Colour figure can be viewed at wileyonlinelibrary.com]

Table II. Characteristics of patients who required hospitalization classified according to the WHO stratification.

Type of infection	Definition	No (%)	Symptoms	Type of TKI	Discontinuation of TKI during infection	Death
Mild	Symptomatic but no pneumonia or hypoxia	21 (9·6%)	18 fever + respiratory symptoms 3 cough + respiratory symptoms	Imatinib 9 Nilotinib 5 Dasatinib 5 Bosutinib 2	3 patients (14%)	2 patients (9·5%)
Moderate	Pneumonia without hypoxia	18 (8·2%)	13 fever + respiratory symptoms 5 cough + respiratory symptoms	Imatinib 11 Nilotinib 3 Dasatinib 2 Bosutinib 2	3 patients (16·6%)	6 patients (75%)
Severe/ critical	Pneumonia and hypoxia Acute life-threatening organ dysfunction	8 (3·6%)	6 fever + respiratory symptoms 2 cough + respiratory symptoms	Imatinib 7 Dasatinib 1	2 patients (25%)	4 patients (50%)

TKI, tyrosine kinase inhibitor.

professionals, whereas in 30% it was not known. At the time of completing the survey, 14 patients still had an ongoing infection. Twelve patients had died due to SARS-CoV-2 infection, with a mortality rate of 5·5% in the positive cohort and of 0·13% in the whole CML cohort. All remaining patients were alive at the last contact. When analysing the

baseline characteristics of patients who died due to SARS-CoV-2 infection compared to patients who remained alive in univariate analysis, age >65 years (83% vs 70%, $P = 0{\cdot}03$), cough as presenting symptom (50% vs 28%, $P = 0{\cdot}001$), imatinib (92% vs 46%, $P = 0{\cdot}02$) and concomitant cardiovascular disorders (50% vs 13%, $P = 0{\cdot}001$) emerged as predisposing factors. Five patients reported post-infection consequences: one patient suffered from Guillain–Barré syndrome, one patient had a maculopapular rash, one a pulmonary fibrosis, one a bacterial endocarditis and one was diagnosed as having alterations of the microcirculation.

Finally, we asked if the pandemic period had changed the clinical management. Sixteen participants (35%) claimed they performed a nasal swab before the start of a TKI. After starting treatment, only eight centres (18%) continued to perform weekly visits as scheduled, 22 centres (49%) reduced them to every two weeks and 15 centres (33%) to one monthly visit. As to the molecular monitoring, 11 centres (24%) monitored residual disease in patients with stable disease less frequently than previously scheduled. More than half of the participants (52%) have not proposed treatment discontinuation during the pandemic and in patients already off therapy 13% were not monitored as previously scheduled.

Discussion

As of 30 August 2021, there have been over 216 million confirmed cases worldwide and over 4·49 millions reported deaths due to COVID-19. The majority of recorded cases presented as asymptomatic or with mild symptoms, while a small percentage of cases showed a severe or critical clinical course and outcome. Older patients with underlying diseases are more susceptible to a severe illness and death[8]; several cases of life-threatening infections have been recorded among healthy individuals with no health-related concerns.[8] A recent retrospective study analysed the mortality rate and the potential predictive parameters in a multicentric large cohort of patients with haematologic malignancies in Italy.[2] The study enrolled 536 patients; at the time of the report, 440 patients had completed the clinical course of the infection and 198 (37%) died. The mortality ratio was compared to that of the general population showing a ratio of 2·04 in the whole cohort and of 3·72 in haematologic patients younger than 70 years. Indeed, if compared to the non-COVID-19 haematologic cohort, the standardized mortality ratio was 41·3. A diagnosis of acute myeloid leukaemia, non-Hodgkin lymphoma (both aggressive and indolent) and plasma cell neoplasms were associated with a worse overall survival. Among 83 myeloproliferative neoplasms recorded in the study, 11 were CML on treatment with TKIs and all were alive at the data cut-off point, whereas four of the nine patients with polycythaemia vera and myelofibrosis who had received ruxolitinib had died.[2]

The present study reports for the first time the impact of the COVID-19 pandemic on a very large cohort of CML patients (8 665) with prospective data referring to a one-year observation period (February 2020–January 2021). The overall incidence is low compared to other haematologic malignancies, highlighting the potential role of TKIs.[2] In fact, a possible impact of TKIs has been hypothesized *in vitro*: imatinib seems to have a role in blocking the fusion of the protein S of the coronavirus belonging to the viral surface with cell membranes.[9] This role could prevent the endocytosis needed for the viral activation of different viral species [SARS-CoV, Middle East respiratory syndrome-related coronavirus (MERS-CoV) and infectious bronchitis virus (IBV)].[10] It is worth recalling that few cases of SARS-CoV-2 infections have also been reported among patients affected by Ph-positive acute lymphoblastic leukaemia (Ph+ ALL) treated with TKIs.[11] Information on 267 patients with Ph+ ALL has been collected, the majority from the regions most affected by phase 1 of the pandemic in Italy. Only one patient proved affected by COVID-19, reinforcing the hypothesis that patients treated with only TKIs have a reduced rate of SARS-CoV-2 infection.[12] In this respect, it is worth recalling that CML is the only haematologic malignancy virtually managed only by targeted treatment. Moreover, it has been demonstrated that TKIs not only reduce the viral replication rate but also upregulate several genes with antiviral action (CD28, IFNγ), while genes with a possible pro-viral action (*ARG-1*, *FUT4*, *CEACAM1*) are expressed less.[13] Despite this biological and clinical evidence, we have to consider that the more favourable outcome of CML patients may also be contributed by the increased mortality observed in other haematologic malignancies because of the treatment received (chemoimmunotherapy in lymphomas), of the disease/treatment-related complications (acute leukaemias and myelodysplastic syndromes) and of the disease-related immune impairment (e.g. multiple myeloma, chronic lymphocytic leukaemia).

At the last American Society of Haematology (ASH) meeting, the CANDID study was presented by the International CML foundation (iCMLf)[14]: a case collection of 110 SARS-CoV-2-positive patients observed among 12·336 CML patients in 20 countries was reported, with an incidence of 0·89%. Similar to our study, the median age at COVID-19 diagnosis was 54 years (in our study the majority of patients were in the age range between 50 and 65 years), with a 55% male prevalence (73% in our series) and with a median time from diagnosis of seven years (six years in our study). Compared to the CANDID study, in our experience more patients presented with a completely asymptomatic form: only 3·6% of patients were diagnosed as having a critical and severe infection requiring assisted mechanical ventilation compared to 17% in the multicentric worldwide cohort. A similar percentage of patients discontinued TKI therapy due to the SARS-CoV-2 infection: 23% in our study *versus* 30% in the CANDID study. The mortality rate reported in our series appears low (5·5%) if compared to that of the CANDID study (14%), in line with that described in other reports

focussing on myeloproliferative neoplasms,[5–8] but higher than the mortality rate of the whole Italian population not affected by haematologic malignancies (2·97%) during the first year of the pandemic.[15] In the iCMLf analysis, a univariate analysis was carried out to define predictive factors associated with an increased mortality rate: age over 75 years, the severity of SARS-CoV-2 infection as graded by the WHO and imatinib therapy were associated with a significantly higher and significant mortality. The increased mortality with imatinib compared to second-generation inhibitors is not surprising considering that the drug is predominantly prescribed to the elderly population with CML. In our study advanced age, concomitant cardiovascular comorbidities and imatinib treatment were indeed associated with an increased mortality due to SARS-CoV-2 infection.

Some groups have attempted to carry out an extensive serological investigation of a possible SARS-CoV-2 infection, testing large CML cohorts. Bonifacio *et al*. reported at the last ASH meeting the infection prevalence in 564 patients in different phases of the disease.[16] Eleven patients resulted IgG-positive, with only three having a previous diagnosis of SARS-CoV-2 infection. Anosmia, ageusia, fever and asthenia were the symptoms most frequently associated with the IgG-positive status. The UK group tested 161 CML patients with diaminobenzoic acid (DABA) analysis and 18 proved positive (11·2%). At diagnosis, 15 patients were asymptomatic or had only mild symptoms: as in the previous study, the most frequent symptoms associated to IgG positivity were fever, cough and fatigue.[17] A large analysis on the possible association with COVID-19, by the Italian Campus CML network, is currently under way.

Based on the results of our survey, we could document some consequences related to the SARS-CoV-2 infection in five patients, but not the so-called 'long-COVID' sequelae.[18] None of the cohorts so far reported have observed long-term sequelae and an analysis focussed on this aspect needs to be planned.

We could also show that the COVID-19 pandemic has had an impact on the management of the disease: about 24% of centres changed the schedule for the molecular monitoring of patients already in molecular response and more than half of the participants did not propose a treatment discontinuation strategy considering the impossibility of carrying out the required close molecular monitoring at least for the first six months.

In conclusion, this study reports for the first time what has occurred to a large cohort of CML patients in Italy during this first year of the COVID-19 pandemic: the mortality rate in CML appears lower if compared to other haematologic malignancies and most patients were occasionally diagnosed as having the infection while being completely asymptomatic. A long-term follow-up is required in order to conclusively define the impact of the pandemic and the possible repercussions of the infection on the efficacy of drugs and on side effects.

References

1. He W, Chen L, Chen L, Yuan G, Fang Y, Chen W, et al. COVID-19 in persons with hematological cancers. *Leukemia*. 2020;**34**(6):1637–45.
2. Passamonti F, Cattaneo C, Arcaini L, Bruna R, Cavo M, Merli F, et al. Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicenter, cohort study. *Lancet Hematology*. 2020;**7**(10):e737–45.
3. Li W, Wang D, Guo J, Yuan G, Yang Z, Gale RP, et al. COVID-19 in persons with chronic myeloid leukemia. *Leukemia*. 2020;**34**(7):1799–804.
4. Breccia M, Abruzzese E, Bocchia M, Bonifacio M, Castagnetti F, Fava C, et al. Chronic myeloid leukemia management at the time of the COVID-19 pandemic in Italy. A campus CML survey. *Leukemia*. 2020;**34**(8):2260–1.
5. Ector GICG, Huijskens EGW, Blijlevens NMA, Westerweel PE. Prevalence of COVID-19 diagnosis in Dutch CML patients during the 2020 SARS-CoV2 pandemic. A prospective Cohort study. *Leukemia*. 2020;**34**(9):2533–5.
6. Başcı S, Ata N, Altuntaş F, Yiğenoğlu TN, Dal MS, Korkmaz S, et al. Outcome of COVID-19 in patients with chronic myeloid leukemia receiving tyrosine kinase inhibitors. *J Oncol Pharm Pract*. 2020;**26**(7):1676–82.
7. Cross NCP, White HE, Colomer D, Ehrencrona H, Foroni L, Gottardi E, et al. Laboratory recommendations for scoring deep molecular responses following treatment for chronic myeloid leukemia. *Leukemia*. 2015;**29**(5):999–1003.
8. Samadizadeh S, Masoudi M, Rastegar M, Salimi V, Shahbaz MB, Tahamtan A. COVID-19: why dose disease severity vaty among individuals? *Respir Med*. 2021;**180**:106356.
9. Coleman CM, Sisk JM, Mingo RM, Nelson EA, White JM, Frieman MB. Abelson kinase inhibitors are potent inhibitors of severe acute respiratory syndrome coronavirus and Middle East respiratory syndrome coronavirus fusion. *J Virol*. 2016;**90**:8924–33.
10. Sisk JM, Frieman MB, Machamer CE. Coronavirus S protein-induced fusion is blocked prior to hemifusion by Abl kinase inhibitors. *J Gen Virol*. 2018;**99**:619–30.
11. Foà R, Bonifacio M, Chiaretti S, Curti A, Candoni A, Fava C, et al. Philadelphia-positive acute lymphoblastic leukemia (ALL) in Italy during the COVID-19 pandemic: a Campus ALL study. *Br J Haematol*. 2020;**190**:e3–5.
12. Nguyen DD, Gao K, Chen J, Wang R, Wei GW. Potentially highly potent drugs for 2019-nCoV. *bioRxiv*. https://doi.org/10.1101/2020.02.05.936013
13. Galimberti S, Petrini M, Baratè C, Ricci F, Balducci S, Grassi S, et al. Tyrosine kinase inhibitors play an antiviral action in patients affected by chronic myeloid leukemia: a possible model supporting their use in the fight against SARS-CoV-2. *Front Oncol*. 2020;**10**:1428.
14. Rea D, Mauro MJ, Cortes JE, Jiang Q, Pagnano KB, Ongondi M, et al. COVID-19 in patients with chronic myeloid leukemia: results from the international CML Foundation (iCMLf) CML and COVID-19 (CANDID) study. *Blood*. 2020;**136**(s1):649.
15. Ministry of Health. Characteristics of COVID-19 patients dying in Italy. Available from: Epicentro.iss.it/en/coronavirus/sars-cov-2-analysis-of-deaths
16. Bonifacio M, Binotto G, Tiribelli M, Miggiano MC, Trawinska MM, Scaffidi L, et al. Serological prevalence of Sars-Cov2 infection among chronic myeloid leukemia patients undergoing tyrosine kinase inhibitor treatment in Italy (COVID-19-HEM study). *Blood*. 2020;**136**(s1):1235.
17. Claudiani S, Rosadas C, McClure M, Khan M, Tedder RS, Innes AJ, et al. Prevalence of SARS-Cov2 infection in patients with chronic myeloid leukemia. *Blood*. 2020;**136**(s1):3065.
18. Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, et al. Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *J Med Virol*. 2021;**93**:1013–22.