



Chronic myelogenous leukemia

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

Massimo Breccia¹ · Elisabetta Abruzzese² · Monica Bocchia³ · Massimiliano Bonifacio⁴ · Fausto Castagnetti⁵ · Carmen Fava⁶ · Sara Galimberti⁷ · Antonella Gozzini⁸ · Gabriele Gugliotta⁵ · Alessandra Iurlo⁹ · Roberto Latagliata¹ · Luigiana Luciano¹⁰ · Patrizia Pregno¹¹ · Giovanna Rege-Cambrin¹² · Gianantonio Rosti⁵ · Fabio Stagno¹³ · Mario Tiribelli¹⁴ · Robin Foà¹ · Giuseppe Saglio⁶ · on behalf of the Campus CML working group

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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

Members of the Campus CML working group are listed below
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✉ Robin Foà
rfoa@bce.uniroma1.it

- ¹ Department of Precision and Translational Medicine, Sapienza University, Rome, Italy
- ² Hematology, Sant'Eugenio Hospital, Rome, Italy
- ³ UOC Hematology, University of Siena, Siena, Italy
- ⁴ Hematology, Policlinico GB Rossi, University of Verona, Verona, Italy
- ⁵ Department of Hematology/Oncology, University of Bologna, Bologna, Italy
- ⁶ Azienda Ospedaliera Mauriziano, Torino, Italy
- ⁷ University of Pisa, Pisa, Italy
- ⁸ Ospedale Careggi, Firenze, Italy
- ⁹ Fondazione IRCS Ca' Granda Ospedale Maggiore Policlinico of Milan, Milan, Italy
- ¹⁰ Federico II University, Naples, Italy
- ¹¹ Ospedale Città della Salute e della Scienza, Turin, Italy
- ¹² Ospedale San Luigi, Orbassano, Italy
- ¹³ Ospedale Ferrarotto-University of Catania, Catania, Italy
- ¹⁴ University of Udine, Udine, Italy

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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Campus CML working group Miggianno Maria Cristina¹⁵, Capodanno Isabella¹⁶, Accurso Vincenzo¹⁷, Sorà Federica¹⁸, Luzi Debora¹⁹, Annunziata Mario²⁰, Attolico Immacolata²¹, Malato Alessandra²², Sancetta Rosaria²³, Elena Chiara²⁴, Barulli Sara²⁵, Scortechini Anna

Rita²⁶, Leonetti-Crescenzi Sabrina²⁷, Tafuri Agostino²⁸, Cavazzini Francesco²⁹, Caocci Giovanni³⁰, Lucchesi Alessandro³¹, Rapezzi Davide³², Pizzuti Michele³³, Binotto Gianni³⁴, Intermesoli Tamara³⁵, Maggi Alessandro³⁶, Crisa' Elena³⁷, Crugnola Monica³⁸, D'Adda Mariella³⁹, Beltrami Germana⁴⁰, Lunghe Francesca⁴¹, Vincelli Iolanda-Donatella⁴², Sanpaolo Grazia⁴³, Franceschini Luca⁴⁴, Russo Sabina⁴⁵, La Barba Gaetano⁴⁶, Levato Luciano⁴⁷

¹⁵U.O.C. Ematologia, Vicenza, Italy; ¹⁶Az. Unità Sanitaria IRCCS Reggio-Emilia, Reggio-Emilia, Italy; ¹⁷UOC Ematologia Policlinico Paolo Giaccone Palermo, Palermo, Italy; ¹⁸Università Cattolica-Policlinico A. Gemelli, IRCCS, Roma, Italy; ¹⁹Oncoematologia-Azienda Ospedaliera Santa Maria, Terni, Italy; ²⁰Az. Ospedaliera Cardarelli, Napoli, Italy; ²¹Ematologia con Trapianto Policlinico Bari, Bari, Italy; ²²UOC Ematologia ad indirizzo oncologico Ospedali Riuniti Villa Sofia-Cervello, Palermo, Italy; ²³UO Ematologia OC dell'Angelo Mestre-Venezia, Venezia- Mestre, Italy; ²⁴Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; ²⁵U.O.C. Ematologia, Pesaro, Italy; ²⁶Clinica Ematologia, Ancona, Italy; ²⁷azienda ospedaliera San Giovanni-Addolorata, Roma, Italy; ²⁸S. Andrea - Sapienza -Azienda Ospedaliera Universitaria, Roma, Italy; ²⁹Az. Ospedaliero-Universitaria S. Anna Ferrara, Ferrara, Italy; ³⁰Ospedale Businco, Cagliari, Italy; ³¹Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; ³²S.C. Ematologia A.S.O. Santa Croce e Carle di Cuneo, Cuneo, Italy; ³³Ematologia Ospedale San Carlo, Potenza, Italy; ³⁴UOC Ematologia ed Immunologia Clinica- Università di Padova, Padova, Italy; ³⁵Papa Giovanni XXIII, Bergamo, Italy; ³⁶s.c. ematologia con trapianto, Taranto, Italy; ³⁷AOU Maggiore della Carità, Novara, Italy; ³⁸AOU Parma, Parma, Italy; ³⁹U. O. Ematologia, Brescia, Italy; ⁴⁰U.O Ematologia Ospedale Policlinico S. Martino, Genova, Italy; ⁴¹Ospedale San Raffaele MI, Milano, Italy; ⁴²divisione di ematologia ospedale Bianchi -Melacrinò-Morelli, Reggio-Calabria, Italy; ⁴³Ematologia Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy; ⁴⁴Policlinico Tor Vergata, Roma, Italy; ⁴⁵AOU G. Martino Policlinico di Messina, Messina, Italy; ⁴⁶Ematologia Clinica Ospedale Civile "Spirito Santo", Pescara, Italy; ⁴⁷Ematologia Catanzaro, Catanzaro, Italy

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