

AML and Covid-19 virus

Induction and consolidation therapy in acute myeloid leukemia (AML) patients results in a high risk of infectious complications. In particular, severe and prolonged neutropenia with neutrophil counts below 500/ μ l or even 100/ μ l leads to an increased risk of febrile complications, due in most cases to bacterial or fungal infections (1). Respiratory virus infections can also occur in AML patients, particularly during seasonal outbreaks, and their recognition has been facilitated by the recent widespread use of molecular microbiologic testing. Their incidence varies widely between 1% and 50% in different series and for different respiratory viruses. Progression from an upper respiratory tract infection (URTI) to a lower respiratory tract infection (LRTI), with frequent bacterial and fungal co-infections, is associated with an increased likelihood of fatal outcome, reported in 5-54% of cases. The respiratory viruses most frequently associated with an adverse prognosis are influenza, parainfluenza, respiratory syncytial virus, adenovirus and human metapneumovirus (2). Although human Coronavirus (HCoV) has not been considered among the most aggressive respiratory viruses, there have also been well-documented cases of severe and even fatal LRTI in HCoV+ hematologic patients (3,4). While these complications would suggest the use of antiviral prophylaxis, the benefit of such an approach remains unproven; it is therefore neither recommended nor utilized in most institutions and viral surveillance seems to be more appropriate in acute lymphoblastic leukemia than in AML (5,6). The Covid-19 is affecting 207 territories around the world and causes illnesses ranging from the common cold to more severe diseases mimicking the Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). The clinical characteristics of the Covid-19 epidemic are being actively studied (6). At difference with the most common respiratory viruses, it is frequently complicated by bilateral interstitial alveolar pneumonia and respiratory insufficiency whose pathogenesis is sustained by a marked cytokine release syndrome. A worldwide rise in the number of daily confirmed cases has led the World Health Organization (WHO) to declare its spread as a global pandemic. We would thus expect that an increasing number of patients with different hematologic malignancies including AML will present with concomitant Covid-19 positivity. No results were found by imputing AML and Covid-19 in the NCBI Pub Med. In addition, no specific recommendations have so far been provided by scientific societies and nothing is known also considering the recent Chinese or Italian experience outbreak. Notwithstanding, a number of questions need to be considered, mainly if the number of Covid-19+ subjects will continue to increase in the general population.

Questions

- a) Should all newly diagnosed patients with AML be tested?
Yes
- b) During the follow-up, should the testing for Covid-19 be limited to patients with respiratory symptoms and/or fever, or should they be tested regularly?
All patients should be tested regularly.
- c) Which induction therapy should be considered in AML Covid-19+ young adult patients?
In young adult asymptomatic patients, standard induction therapy should be considered; in symptomatic patients the combination of venetoclax plus hypomethylating agents (VEN/HMA) could be preferable.
- d) What about older patients? Should Covid-19 positivity be considered a criteria of unfitness to intensive or even to less intensive approaches like VEN/HMA?
Older Covid-19 positive patients, regardless of symptoms, could be considered for VEN/HMA.
- e) Should high-dose cytarabine-based consolidation therapy be administered to Covid-19+ patients achieving complete remission or should a dose reduction be considered?
Intermediate dose ARA-C should be considered; in symptomatic patients, consolidation should be delayed up to resolution of symptoms.
- f) What kind of isolation should be used to protect AML patients as well as other patients and health care workers?
Patients should be managed in COVID unit by experienced hematologists in collaboration with pneumologists and intensivists; alternatively, a single room with negative pressure could be considered.
- g) Which treatment for relapsed patients?
Prefer molecularly targeted therapies whenever possible: gilteritinib for FLT3+ patients, Ivosidenib and Enasidenib for patients with IDH1 and IDH2 mutations, respectively; alternatively, chemotherapy may be an option in young adults. For older patients with relapse after intensive chemo, consider HMA+/-VEN; for patients relapsing after VEN/HMA consider best supportive care.
- h) Should allogeneic transplants be performed?
An allogeneic transplant program should be deferred until complete resolution of all symptoms of COVID-19 and after at least one month from documented SARS-CoV-2 negativization. The potential contribution of anti-SARS-CoV-2 antibody detection is presently unclear

We would like to open a debate on these topics, which could be useful for the hematologic community helping to manage Covid-19+ AML patients at the best of different possibilities and in a uniform manner.

Felicetto Ferrara, #Robin Foà, ° Adriano Venditti and *Giuseppe Rossi

Division of Hematology, Cardarelli Hospital, Naples, Italy; # Hematology, Sapienza University, Rome, Italy; ° Hematology, Tor Vergata University, Rome, Italy; *Division of Hematology, Spedali Civili Brescia, Italy

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