Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Introduction

The severe acute respiratory syndrome-coronavirus 2 (SARS-CoV2) is an RNA virus which has led to an ongoing global pandemic.\(^1\) Since its first description in December 2019, it has caused over 68 million infections and 1.5 million deaths over a 1-year period. Illness caused by this virus (named Coronavirus disease-2019, or COVID-19 for short), can present as a spectrum from an asymptomatic carrier state to respiratory failure and multi-organ dysfunction.\(^2\) The COVID-19 pandemic is an unprecedented crisis, and demonstrates a case fatality rate of approximately 5% to 7%.\(^3\) The case fatality rate underestimates the burden of infection, as patients with mild or asymptomatic disease are excluded, which may constitute over 50% of all cases. A better measure is provided by the infection fatality rate, which is estimated to range from 0% to 1.6%.\(^4\) Meta-analysis of clinical data has shown that approximately 30% of patients require intensive care unit admission, and the mortality rate in this subset approaches 39%.\(^5\) The risk of severe disease and mortality is higher is certain subgroups, including those with comorbidities, active malignancy, or advanced age (> 60 years).\(^6\)

Owing to disease and treatment-related factors, patients with cancer are at an especially high risk of severe disease and have been noted to have a mortality rate exceeding 25%.\(^7,8\) This initial surge in mortality in patients with cancer prompted several groups to recommend delay or deferral of curative chemotherapy to minimize the risk of mortality owing to severe COVID-19.\(^9\) However, delays in treatment of patients with hematologic malignancies, especially those with acute leukemia planned for chemotherapy or transplantation, are associated with a risk of disease progression and inferior outcomes. For these patients, added efforts must be made to minimize infection risk while ensuring continuation of treatment. A judicious modification of protocols at each stage of treatment to minimize the risk of infection must be attempted, depending on disease status and local factors.\(^10\) We provide a focused review on the current evidence and recommendations for management of patients with acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) during the COVID-19 pandemic.

Patients With Hematologic Malignancies are Predisposed to COVID-19 and Have Distinctly Poorer Outcomes

Dysregulation of several components of innate and acquired immunity is noted in most malignancies.\(^11\) Patients with AML have higher expression of negative regulatory receptors and proliferation of regulatory T cells.\(^12\) This is potentiated by disruption of normal NK cell development and defective metabolism, further attenuating the host response.\(^13\) Patients with AML have an added risk owing to myelosuppression and myeloid dysfunction, and patients with ALL have an added risk owing to hypogammaglobulinemia and
prolonged use of steroids. All these factors work in tandem to increase the risk of various viral and fungal infections, including uncommon pathogens in patients with acute leukemia. The highest risk of COVID-19 infection has been noted with ALL, followed by essential thrombocytenosis and AML. This surprising finding indicates the undefined role of many factors beyond myelosuppression in mediating the risk of infection and disease.

From the beginning of 2020, several reports indicated a higher risk of mortality with COVID-19 in patients with cancer. However, as treatment of acute leukemia can often not be delayed, COVID-19 infections were documented in several patients with hematologic cancers, providing valuable insights into infection risk and outcomes. The largest body of data is available from 3 studies, summarized in Table 1. The first study is a database review from Turkey, which included all patients with COVID-19 infection from a national database. Of a total of 188,897 patients, 740 were noted to have concurrent COVID-19 and hematologic malignancy. This subset of patients was compared with another 740 patients with COVID without hematologic malignancies and found to have a 2-fold higher mortality (13.8% vs. 6.8%). The second study is a large retrospective database analysis of United States health records, which compared outcomes with hematologic malignancies in patients who were diagnosed recently versus historic cohorts. This study included 73 million records and identified 17,000 patients with COVID-19, of whom 420 had co-existent blood cancer. A significantly higher risk of death was noted in patients with COVID-19 compared with those without COVID. The third is a meta-analysis that included 3377 patients and demonstrated an initial mortality of 34% for all patients with hematologic cancers, which was much higher for patients > 60 years of age. Similar data has also become available from low- and middle-income settings, indicating the importance of low-cost infection control measures in resource-constrained settings. In a large tertiary care center from India, 7043 patients with cancer were screened, out of which 230 patients (hematologic malignancies, 37%) had concurrent COVID-19 while receiving active treatment. This subgroup was noted to have a relatively high 30-day mortality of 10%, much higher than the case fatality rate with COVID-19 in general. A majority of patients in this subgroup had mild COVID-19, and outcomes with severe disease are expected to be worse. Further data is expected from the COVID Hematologic Cancer Registry of India (The CHCRI Study), which has accrued 277 patients as of December 2020.

### Table 1: Salient Features of the Largest Datasets on Outcomes of Patients With COVID-19 Infection and Hematologic Malignancies

| Reference | Study and Total Patients Included | Patients With COVID-19 and Hematologic Cancers | Fatality Rate, % | Others |
|-----------|----------------------------------|-----------------------------------------------|-----------------|--------|
| 18        | National Turkish Database of COVID-19 patients: 188,897 patients with COVID-19 from database | 740 | 13.8 | Higher rates of severe disease, hospital stay, and ventilator requirement in this group compared with COVID-19 without hematologic cancers (mortality, 13.8% vs. 6.8%)
| 15        | Electronic Health Record Screening: 73 million EHRs screened, 17,130 with COVID-19 | 420 | 14.8 | Death rate for COVID-19 alone was 5.1% and hematologic malignancies without COVID was 4.1% |
| 19        | Meta-analysis, 3377 patients across 39 studies | 3377 | 34 | Mortality in patients < 60 y: 25% Mortality in patients > 60 y: 47% Mortality in pediatric age group: 4% |

Abbreviations: COVID-19 = coronavirus disease-2019; EHR = electronic health record.

### Table 2: Summary of Recommendations to Further Reduce the Risk of COVID-19 Infection or Severe Disease in Patients with Leukemia

| Acute Myeloid Leukemia | Acute Lymphoblastic Leukemia |
|------------------------|------------------------------|
| COVID-19 testing before starting treatment | COVID-19 testing before starting treatment |
| Continue environmental precautions | Continue environmental precautions |
| Young patients: full dose induction chemotherapy | Full dose induction (with steroids) |
| Reduce HDAC to 1.5 g/m² per dose | Reduce anthracycline dose for those at high risk of infection |
| Higher transfusion cutoff | Outpatient management of post-induction cycles |
| Minimize hospital stay by discharging early | Use TKIs as much as possible for Ph-positive ALL |

Abbreviations: ALL = acute lymphoblastic lymphoma; COVID-19 = Coronavirus disease-2019; HDAC = high-dose cytarabine; Ph = Philadelphia chromosome; TKI = tyrosine kinase inhibitor.
management of patients following intensive chemotherapy for AML has been found to be safe and feasible if close follow-up after discharge is maintained.\textsuperscript{29,30} Patients on outpatient follow-up with neutropenia must be educated about risks of neutropenia and the need for re-admission in case of fever or development of new symptoms.\textsuperscript{31} In-hospital stay constitutes the largest proportion of the initial cost of AML induction independent of blood product usage, and the above measures should also help in reducing costs.\textsuperscript{32} Patients who develop febrile neutropenia should be re-tested for COVID-19 if no other focus of infection is found, as COVID-19 reverse transcription polymerase chain reaction (RT-PCR) can be falsely negative in the initial stages of infection.\textsuperscript{33}

Patients classified as low-risk AML continue with consolidation chemotherapy with high-dose cytarabine, and those as intermediate or high risk are candidates for stem cell transplantation.\textsuperscript{27} For patients who are elderly, unfit, or otherwise not candidates for intensive chemotherapy, treatment with hypomethylating agents, preferably with the addition of venetoclax, is recommended.\textsuperscript{35} For consolidation with high-dose cytarabine, the AML 15 trial provides evidence for reducing the dose of high-dose cytarabine from 3 g/m$^2$ to 1.5 g/m$^2$, which reduces the duration of neutropenia while achieving similar outcomes.\textsuperscript{35}

COVID-19 lends significant challenges to transfusion services, leading to a blood component shortage and the potential for donor or staff infection.\textsuperscript{36} Even in developed countries, a shortage of blood components and reduction in voluntary donations has been documented.\textsuperscript{37} To reduce the burden on supportive care, a higher threshold for transfusion support is recommended. A threshold of 7 g/dL before blood transfusion in AML is associated with comparable length of hospital stay, mortality, and treatment response rates while reducing resource utilization.\textsuperscript{38} Likewise, a lower platelet cut off of 10,000/ul rather than 20,000/ul before prophylactic transfusion is safe and cost-effective without increasing the risk of bleeding.\textsuperscript{39}

Specific Recommendations for ALL

The ASH also provides expert recommendations on management of ALL during the COVID-19 pandemic. For patients with Ph-negative ALL, the usual induction doses of steroids are advised. The initial concerns about worsening COVID-19 disease with steroids have been alleviated with demonstration of safety and efficacy of steroids in treating severe COVID-19.\textsuperscript{40} Many experts recommend lowering anthracycline doses by 50% and using granulocyte colony stimulating factor to hasten count recovery to reduce the duration of myelosuppression. As anthracyclines contribute vitally to the efficacy of the induction regimen, this decision should be taken after thorough consideration.\textsuperscript{41} While continuing subsequent cycles post induction, attempts should be made to administer treatment on an ambulatory basis if feasible. Outpatient treatment following induction has been found to be safe for adult patients with ALL.\textsuperscript{42} In extreme situations and with close monitoring, administration of high-dose methotrexate on an outpatient basis has also been found safe.\textsuperscript{43} An individualized decision to continue subsequent cyclophosphamide, cytarabine, or etoposide on an outpatient basis can be made if patients are expected to comply with instructions on neutropenic care and regular follow-up.\textsuperscript{44} As ALL is a curable disease in many age groups, it is recommended that priority be given to minimizing treatment delays. These principles are even
more pertinent in the pediatric age group, where excellent long-term outcomes are noted with strict compliance to treatment protocols. For patients with ALL on treatment who developed COVID-19, therapy may have to be temporarily halted. The ASH guidelines recommend that treatment delays, if any, must not exceed 2 weeks. A decision to restart or withhold treatment must be made on a patient-by-patient basis, considering the phase of treatment, presence of neutropenia, additional infections, and remission status.

For induction therapy of Ph-positive ALL, anthracyclines can be safely omitted by using a less myelosuppressive combination of vincristine, steroids, and tyrosine kinase inhibitor. For subsequent cycles, tyrosine kinase inhibitors should be continued as far as possible to avoid maximal benefit.

For patients with relapsed ALL, newer non-myelosuppressive options include blinatumomab for B-cell ALL and nelarabine for T-cell ALL, which avoid prolonged cytopenia and the attendant risk of infections. However, availability and cost play a major role before using these drugs, and for most patients in the Indian setting, combination salvage chemotherapy with appropriate precautions may be the only option. Table 2 summarizes recommendations for management of AML and ALL during COVID-19.

**Stem Cell Transplantation**

Indications for stem cell transplantation in acute leukemia include high-risk disease (based on cytogenetic and mutation data or inadequate response to therapy) or refractory disease.

Patients with AML who need a transplant should be referred as soon as possible, as a delay leading to even minimal residual disease positivity is associated with disease progression and inferior survival. It must be emphasized that the risk of donor to patient transmission of COVID-19 is low, and blood-borne transmission has not yet been documented despite the presence of low-level viremia. However, if a donor tests positive for COVID-19, temporary deferral is universally advised. The European Bone Marrow Transplantation (EBMT) guidelines recommend a 3-month deferral if a donor tests positive for COVID-19, and a 28-day deferral in case of a potential exposure to an infected individual. It is vital to adapt these guidelines to local practice, as a delay of 1 to 3 months may not be feasible for certain high-risk patients. This principle is mirrored in the American Society for Transplantation and Cellular Therapy (ASTCT) guidelines, which recommend consideration of a donor with recent infection after 28 days on a case-by-case basis.

**Our Center’s Data on COVID-19 and Hematologic Malignancies**

We recently submitted data on in-patient management of hematologic cancers from our center, a 99-bed cancer unit of a 1600-bed teaching hospital (National Medical Journal of India, Manuscript 620_20, under issue preparation). The data has been updated since then, and the following is a short summary highlighting the steps taken to mitigate the risk of COVID-19 in this patient subset.

Owing to necessity and urgency of treatment, hematology-oncology services continued as usual after the onset of the pandemic, and stem cell transplantation services restarted in June 2020 after a 3-month interval.

Preventive measures for infection control included the following:

1. **Health care staff**
   a. Provision of personal protective equipment for all health care staff (plastic fronted gowns, masks, and face shields) provided by the hospital.
   b. Screening before entering the premises with an infrared thermometer. Those with fever, upper respiratory symptoms, or a history of potential contact were triaged according to risk of exposure. High-risk contacts were quarantined for 14 days and retested before joining duty.

2. **Outpatient clinics**
   a. To reduce person-to-person spread, patient numbers in the clinic were capped, and patients were shifted to telemedicine at the discretion of the primary physician.
   b. For patients, mandatory testing with nasal swab for COVID-19 RT-PCR was done before admission, and

---

**Table 3** Our Institutional Data on Patients With Hematologic Malignancies Managed In-patient During the COVID-19 Pandemic

|                    | N   | Median Age (Range), y |
|--------------------|-----|----------------------|
| AML                | 17  | 35 (20-73)           |
| ALL                | 15  | 35 (14-75),          |
| Stem cell transplantation | 12  | 39.5 (10-60) |
| Lymphoma (all subtypes) | 22  | 46 (23-66)  |
| Myeloma with complications | 2   | 70 (68-72)  |
| Total             | 68  |                      |

| Patients With COVID-19 Infections and Details | Patient Deaths Owing to COVID-19 |
|-----------------------------------------------|----------------------------------|
| 3 Pt 1: APL at presentation with type 1 respiratory failure | Pt 1 died owing to progressive respiratory failure before treatment could be started |
| 2 Pt 2: AML in peak cytopenia with respiratory failure | Pt 2 died of worsening respiratory failure in peak cytopenia |
| 1 Pt 3: AML post induction with normal counts prior to starting HiDAC | 0 |
| Pt 4: B-ALL at diagnosis, skipped daunorubicin, uneventful recovery | 0 |

Abbreviations: ALL = acute lymphoblastic lymphoma; AML = acute myeloid leukemia; APML = acute promyelocytic leukemia; B-ALL = B-cell acute lymphoblastic leukemia; COVID-19 = Coronavirus disease-2019; HiDAC = high-dose cytarabine; Pt = patient.
patients were admitted in a temporary pre-COVID area before shifting to wards.

c. If found positive, patients were shifted to isolation wards or home quarantine as decided by the infectious diseases team.

d. Those who developed respiratory symptoms or hypoxia in-hospital were re-tested with high-resolution computed tomography of the chest and nasal swab and shifted temporarily to a pre-COVID holding area until reports were ready.

e. Strict visitor restriction was placed, and only 1 visitor was allowed in the hospital.

(3) High-risk areas (leukemia wards and stem cell transplantation)

a. In bone marrow transplantation, mandatory testing of stem cell donors and family members was performed. No visitors were allowed inside with the exception of pediatric patients, and visitation was done by iPad or mobile phones.

b. Surface cleaning of high-traffic surfaces was performed every 6 hours according to protocol.

All necessary measures as listed above were broadly followed, and no dose reduction was done for any patient unless otherwise indicated. Since April 2020, a total of 68 adult patients were admitted in the hospital for treatment of hematologic malignancies, including 56 for chemotherapy and 12 for stem cell transplantation. The above experience emphasizes the need for active treatment.

Conclusions

The COVID-19 pandemic is an unprecedented event and has adversely affected health care services globally. Management of high-risk cancers and stem cell transplants must continue as before while mitigating the risk of acquiring infection. Several amendments to routine management approach to acute leukemia are recommended by expert groups. These changes, along with basic measures like hand hygiene, surface cleaning, mandatory mask use, social distancing, and reducing hospital stay are effective steps that can permit continuation of treatment while minimizing the risk of COVID-19.

Disclosure

The authors have stated that they have no conflicts of interest.

References

1. Casella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R, Feature, evaluation, and treatment of coronavirus. Treasure Island (FL): StatPearls Publishing LLC; 2020.

2. Cevik M, Bamford CGG, Ho A. COVID-19 pandemic—a focused review for clinicians. Clin Microbiol Infect 2020; 26:842-7.

3. Kahathuduwa C, Dhanaasekara C, Chiu S-H. Case fatality rate in COVID-19: a systematic review and meta-analysis. medRxiv 2020.

4. Ioannidis J. The infection fatality rate of COVID-19 inferred from seroprevalence data. medRxiv 2020.

5. Abate SM, Almeedi A, Mantfardo B, Basu B. Rate of intensive care unit admission and outcomes among patients with coronavirus: a systematic review and meta-analysis. PLos One 2020; 15:e023563.

6. Pascalella G, Strumia A, Páloge C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med 2020; 288:192-206.

7. Saini KS, Tagliamento M, Lambertini M, et al. Mortality in patients with cancer and coronavirus disease 2019: a systematic review and pooled analysis of 52 studies. Eur J Cancer 2020; 139:43-50.

8. Poormanis PM, Guarnieri V, Cardoso M-J. Cancer and COVID-19: what do we really know? Lancet 2020; 395:1884-5.

9. Curtigiano G, Baranee J, Cervantes A, et al, Panel Members. Managing cancer patients during the COVID-19 pandemic: an ESMO multidisciplinary expert consensus. Ann Oncol 2020; 31:1520-35.

10. Paul S, Rausch CR, Jain N, et al. Treating leukemia in the time of COVID-19. Acta Haematologica 2020;1-13.

11. Tian T, Olson S, Whitacre JM, Harding A. The origins of cancer robustness and evolvability. Integr Biol (Camb) 2011; 3:17-30.

12. Wang X, Zheng J, Liu J, et al. Increased population of CD4+ CD25(high) regulatory T cells with their higher apoptotic and proliferating status in peripheral blood of acute myeloid leukemia patients. Eur J Haematol 2005; 75:468-76.

13. Devillier R, Chrétien A-S, Pagliardini T, Salem N, Blaise D, Olive D. Mechanisms of NK cell dysfunction in the tumor microenvironment and current clinical approaches to harness NK cell potential for immunotherapy. J Leukoc Biol 2020; 107:585-604.

14. Wade JC. Viral infections in patients with hematological malignancies. Hematology Am Soc Hematol Educ Program 2006; 2006:368-74.

15. Wang Q, Berger NA, Xu R. When hematologic malignancies meet COVID-19 in the United States: infections, death, and disparities. Blood Rev 2020;100775.

16. Liang W, Guan W, Chen R, et al. COVID-19 infection: a nationwide analysis in China. Lancet Oncol 2020; 21:335-7.

17. Dai M, Liu D, Liu M, et al. Patients with cancer appear more vulnerable to SARS-COV-2: a multicenter study during the COVID-19 outbreak. Cancer Discov 2020; 10:783-91.

18. Yigeonlug TR, Ata N, Alruntas F, et al. The outcome of COVID-19 in patients with hematological malignancy. J Med Virol 2021; 93:1099-104.

19. Vijenthira A, Gong IY, Fox TA, et al. Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3577 patients. Blood 2020; 136:2881-92.

20. Ramanawamy A, Nayak L, Roy Moulik N, et al. COVID-19 in cancer patients on active systemic therapy – outcomes from LMIC scenario with an emphasis on need for active treatment. Cancer Med 2020; 9:8747-53.

21. Esposito S, Principi N, Leung CC, Migliori GB. Universal use of face masks for success against COVID-19: evidence and implications for prevention policies. Eur Respir J 2020; 55:2001260.

22. Hsi TTP, Ngoc PNH, Hai NM, Tuan LA. Effect of the social distancing measures on the spread of COVID-19 in 10 highly infected countries. Sci Total Environ 2020; 742:140430.

23. Waghmare A, Abidi MZ, Boeckh M, et al. Guidelines for COVID-19 management in hematopoietic cell transplantation and cellular therapy recipients. Biol Blood Marrow Transplant 2020; 26:1983-94.

24. Wu S, Wang Y, Jin X, Tian J, Liu J, Mao Y. Environmental contamination by SARS-CoV-2 in a designated hospital for coronavirus disease 2019. Ann J Infect Control 2020; 48:910-6.

25. Gelfach M, Wolff S, Ludwig S, et al. Rapid SARS-CoV-2 inactivation by commonly available chemicals on inanimate surfaces. J Hosp Infect 2020; 106:633-4.

26. Ghapure R, Hunter CM, Schnall AH, et al. Knowledge and practices regarding safe household cleaning and disinfection for COVID-19 Prevention - United States, May 2020. MMWR Morb Mortal Wkly Rep 2020; 69:705-9.

27. Döhner H, Estey E, Grünwade D, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood 2019; 12:129:424-47.

28. Kayal S, Sengar M, Jain H, et al. Induction related mortality in acute myeloid leukemia: multivariate model of predictive score from the Indian Acute Leukemia Research Database (InaARD) of the Hematologic Cancer Consortium (HCC). Eur J Cancer 2019; 134:2615.

29. Mahery FL, Gardner KM, Shannon Dorcy K, et al. Outpatient intensive induction chemotherapy for acute myeloid leukemia and high-risk myelodysplastic syndrome. Blood Adv 2020; 4:611-6.

30. Walter RB, Taylor LR, Gardner KM, Dorcy KS, Vaughn JE, Estey EH. Outpatient management following intensive induction or salvage chemotherapy for acute myeloid leukemia. Clin Adv Hematol Oncol 2013; 11:571-7.

31. Walter RB, Lee SJ, Gardner KM, et al. Outpatient management following intensive induction chemotherapy for myelodysplastic syndromes and acute myeloid leukemia: a pilot study. Haematologica 2011; 96:914-7.
32. Leunis A, Blommestein HM, Huigeni PC, Blijlevens NMA, Jongen-Lavrencic M, Uyl-de Groot CA. The costs of initial treatment for patients with acute myeloid leukemia in the Netherlands. Leuk Res 2013; 37:245-50.
33. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lesler J. Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure. Ann Intern Med 2020; 173:262-7.
34. DiNardo CD, Pratz K, Pullarkat V, et al. Venetoclax combined with decitabine or azacitidine in treatment-naive, elderly patients with acute myeloid leukemia. Blood 2019; 133:7-17.
35. Burnett AK, Russell NH, Hills RK, et al. Optimization of chemotherapy for younger patients with acute myeloid leukemia: results of the medical research council AML15 trial. J Clin Oncol 2013; 31:3360-8.
36. Arcot PJ, Kumar K, Mukhopadhyay T, Subramanian A. Potential challenges faced by blood bank services during COVID-19 pandemic and their mitigative measures: the Indian scenario. Transfus Apher Sci 2020; 59:102877.
37. Stanworth SJ, New HV, Apelseth TO, et al. Effects of the COVID-19 pandemic on supply and use of blood for transfusion. Lancet Haematol 2020; 7:e756-64.
38. Ballo O, Fleckenstein P, Eladly F, et al. Reducing the red blood cell transfusion threshold from 8.0 g/dl to 7.0 g/dl in acute myeloid leukemia patients undergoing induction chemotherapy reduces transfusion rates without adversely affecting patient outcome. Vox Sang 2020; 115:570-8.
39. Sauder R, Di Bona E, Lerede T, et al. Age-adapted moderate-dose induction and flexible outpatient postremission therapy for elderly patients with acute lymphoblastic leukemia. Blood 1996; 88:1521-9.
40. Chatterjee K, Wu CP, Bhardwaj A, Siuba M. Steroids in COVID-19: an overview. Cleve Clin J Med 2020, Online ahead of print.
41. Gottlieb AJ, Weinberg V, Ellison R, et al. Efficacy of daunorubicin in the therapy of adult acute lymphocytic leukemia: a prospective randomized trial by Cancer and Leukemia Group B. Blood 1984; 64:267-74.
42. Basan R, De Bona E, Lerede T, et al. Age-adapted moderate-dose induction and flexible outpatient postremission therapy for elderly patients with acute lymphoblastic leukemia. Leuk Lymphoma 1996; 22:295-301.
43. Bartholomew JL, Dai H, August KJ, Ryan RE, Stegenga KA. Feasibility of outpatient high-dose methotrexate infusions in pediatric patients with B-lineage acute lymphoblastic leukemia. J Adv Pract Oncol 2018; 9:381-6.
44. Møller T, Nielsen OJ, Welinder P, et al. Safe and feasible outpatient treatment following induction and consolidation chemotherapy for patients with acute leukemia. Eur J Haematol 2010; 84:316-22.
45. Demidowicz E, Pogorzala M, Lecka M, et al. Outcome of pediatric acute lymphoblastic leukemia: sixty years of progress. Anticancer Res 2019; 39:5203-7.
46. Lee HJ, Thompson JE, Wang ES, Wetzler M. Philadelphia chromosome-positive acute lymphoblastic leukemia: current treatment and future perspectives. Cancer 2011; 117:1585-94.
47. Brissot E, Labopin M, Baron F, et al. Management of patients with acute leukemia during the COVID-19 outbreak: practical guidelines from the acute leukemia working party of the European Society for Blood and Marrow Transplantation. Bone Marrow Transplant 2020, Online ahead of print.
48. Benjamin JE, Stein AS. The role of blinatumomab in patients with relapsed/refractory acute lymphoblastic leukemia. Ther Adv Hematol 2016; 7:142-56.
49. Kadia TM, Gandhi V. Nelarabine in the treatment of pediatric and adult patients with T-cell acute lymphoblastic leukemia and lymphoma. Exp Rev Hematol 2017; 10:1-8.
50. Saikia T. Challenges in managing acute leukemia in India. Cancer Stat Treat 2020; 3:645-6.
51. Appelbaum FR. Indications for allogeneic hematopoietic cell transplantation for acute myeloid leukemia in the genomic era. Am Soc Clin Oncol Educ Book 2014; 34:e327-33.
52. Buckley SA, Wood BL, Orthus M, et al. Minimal residual disease prior to allogeneic hematopoietic cell transplantation in acute myeloid leukemia: a meta-analysis. Haematologica 2017; 102:865-73.
53. Zhang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. Transfus Med Rev 2020; 34:75-80.
54. Ljungman P, Mikulski M, de la Camara R, et al. European Society for Blood and Marrow Transplantation. The challenge of COVID-19 and hematopoietic cell transplantation; EBMT recommendations for management of hematopoietic cell transplant recipients, their donors, and patients undergoing CAR T-cell therapy. Bone Marrow Transplant 2020; 55:2071-6.