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614.ACUTE LYMPHOBLASTIC LEUKEMIAS: THERAPIES, EXCLUDING TRANSPLANTATION AND CELLULAR IMMUNOTHERAPIES

Newly Dignosed Early T-Cell Precursor Acute Lymphoblastic Leukemia Successfully Treated with Venetoclax Combined with DA and IA Regime

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Abstract

Background: Early T-cell precursor acute lymphoblastic leukemia (ETP-ALL) is a distinctive and extremely aggressive subtype of T-ALL. It is characterized by the aberrant expression of myeloid/stem cell antigens and the lack of Tlymphoid antigens including CD1a, CD4, CD5, and CD8. Currently, standard combination chemotherapy is still the mainstay of ETP-ALL treatment. However, the optimal management remains to be determined. ETP-ALL has low response rates to conventional chemotherapy and high relapse rates with a grim prognosis. Although some ETPALL patients achieved morphologic complete remission (CR), a more signifcant proportion maintained MRD positive. Under the traditional induction and intensifcation treatment strategy, the ETP-ALL group had worse long-term outcomes than the non-ETP-ALL group [1]. A recent preclinical study suggested that inhibition of B-cell lymphoma/leukemia-2 (BCL-2) might be a potential treatment option for patients with ETP-ALL [2]. Here, we present two cases of ETP-ALL clinical reactivity to venetoclax in combination with the IA regimen, providing a better bridge to allogeneic hematopoietic stem cell transplantation (allo-HSCT).

Case 1

A 47-year-old female was diagnosed with ETPALL in October 2021. Flow cytometry analysis showed CD7,CD117,CD34,CD13,CD2,CD200,cyCD3 positive,suggestive of ETP ALL. Cytogenetic analysis was normal and molecular panel identified aberrations in TET, EP300 and EZH2. She then recived venetoclax plus DA regime(venetoclax, 100 mg d1, 200 mg d2, 400 mg qd d3-14;daunorubicin 40mg d1-3;cytarabine 100mg d1-5). A bone marrow biopsy after the 1st cycle revealed CR with minimum residual disease (MRD) 1.91% by flow cytometry. She then received 2nd cycle of venetoclax plus CAG treatment and got MRD negative. She received 2cycles of the same combination and remained in MRD-negative CR prior to proceeding with a reduced intensity haploidentical allo-transplantation. She is currently 1 years and 4 months post-transplant and in remission.

Case 2

A 53-year-old man was diagnosed with ETP-ALL following bone marrow aspiration in August 2022. He presented with Leukopenia and anemia (WBC 2.53× 109 /L, HB 73 g/L, PLT 148 × 109 /L). Bone marrow biopsy revealed a hypercellular bone marrow with 80% lymphoid blasts, negative for MPO staining. The flow cytometry showed the immunophenotype of the lymphoid blasts (CD7+CD34+CD33+CD13+CD200+cyCD3+nTdT+), which were consistent with the immunophenotype of the ETP-leukemic cells. Cytogenetics revealed der(4)(q35).The molecular panel identified aberrations in CSF3R,DNMT3A,CCND3,CSF3R and WT1. Therefore, ETP-ALL was diagnosed. Initially, he received the first cycles of venetoclax combined with IA regimen (venetoclax, 100 mg d1, 200 mg d2, 400 mg qd d3-14;idarubicin 10mg d1-3,cytarabine 100mg d1-5), and CR was achieved this time. Then, he received a 3rd CAG therapy. Subsequently, he underwent hematopoietic stem cell transplantation (HSCT) successfully in December, and CR was still maintained at now 7 months after HSCT.

Conclusion

Combination therapy of venetoclax with IA regimen is an effective regimen for treating patients with ETP ALL.

References

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