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ELEVENTH ANNUAL MEETING

Nelarabine, Etoposide and Cyclophosphamide for adult T cell acute lymphoblastic leukemia/lymphoma relapsing after pediatric-inspired frontline approaches: report of 3 cases from a real-life setting

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INTRODUCTION

T-cell acute lymphoblastic leukemia/lymphoma (T-ALL/LBL) is an aggressive lymphoid malignancy, accounting for ≈ 20% of all ALL cases, with a peak of incidence in childhood. Its clinical presentation includes hyperleukocytosis with frequent extramedullary involvement of lymph nodes and non-lymphoid organs.[1,2] Although current treatment protocols yield complete remission (CR) rates approaching 90% in newly diagnosed adult T-ALL/LBL, approximately half of these patients will experience relapse within the first 2 years.[1] The outcome of adult patients with relapsed/refractory (R/R) T-cell acute lymphoblastic leukemia/lymphoma (T-ALL/LBL) is particularly poor. Nelarabine is the only agent specifically approved for relapsed/refractory T-ALL o and T-LBL in children and adults in Europe.[3] The safety profile and efficacy of nelarabine in R/R T-ALL/LBL have been explored in combination regimens with cyclophosphamide and etoposide (NCE) in children. Its role in adults is less defined. Here we describe the outcome of 3 adult patients treated with NCE.

CLINICAL CASES

Patient 1 was a 22-year-old female with a cortical T-ALL with inv(7)(p15q34;TCRB::HOXA) and delCDKN2AB/9p21. She experienced an early relapse after the frontline treatment according to the NILG ALL 10/07 protocol. Salvage therapy with venetoclax-decitabine was administered with a transient CR before a hematological and extramedullary relapse occurred with left pleural effusion and a plaque-like pleural thickening with subpleural and mammary adenopathies. Subsequently, she was treated with an NCE regimen which was overall well tolerated. She attained morphologic CR with negative MFC-MRD and a chest CT and 18FDG-PET scan was consistent with full treatment efficacy. She proceeded with hematopoietic stem cell transplantation (HSCT) but died before engraftment due to septic shock.

Patient 2 was a 36-year-old male with a cortical T-ALL with TRB::TLX1 rearrangement, delCDKN2AB/9p21, and TP53/17p13. He was treated according to the NILG ALL 10/07 protocol, attaining CR with MFC- MRD negativity after induction, along with remission of extramedullary disease. Prior to the initiation of cycle 5 a bone marrow aspirate documented disease relapse, so the patient was allocated to HSCT from an HLA- matched sibling donor, with a myeloablative conditioning (TBF) regimen. Three years after HSCT the patient relapsed with BM and mediastinal involvement. NCE regimen was administered with good tolerance except for G3 oral mucositis. No neurological side effects were noted (no intrathecal prophylaxis was given). Disease revaluation showed a CR with MFC-MRD negativity and major reduction of the mediastinal mass. Then he received consolidation chemotherapy with high-dose methotrexate and peg-asparaginase and proceeded to a second HSCT but died due to disease relapse.

Patient 3 was a 35-year-old female with a mediastinal T-LBL. She was treated according to the GIMEMA ALL 1913 protocol but experienced an isolated CNS relapse just before maintenance. Thus, we performed biweekly triple intrathecal therapy administrations followed by high-dose cytosine arabinoside and mitoxantrone (HAM) regimen, obtaining CNS1. Soon after, she experienced a leukemic relapse with a concomitant mammary mass, so NCE regimen was offered with a transient peripheral blast clearance and partial reduction of the extramedullary disease. Treatment was well tolerated but led to a prolonged aplastic phase, complicated by sepsis. No signs of neurotoxicity were noted. Shortly after the patient experienced disease progression and died without the possibility to proceed to HSCT.

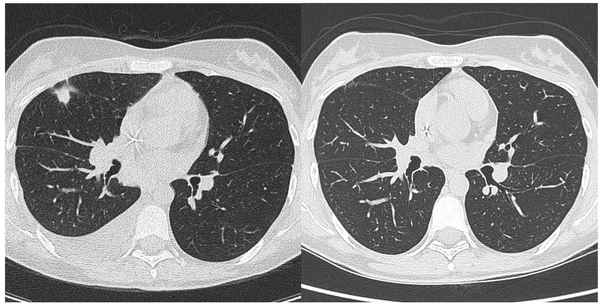


Figure 1a (left) and 1b (left). *Chest CT scan showing mediastinal lymph nodes and pleural involvement before and after treatment with NCE regimen in patient 1*

CONCLUSIONS

Although limited, our experience confirms the clinical activity of NCE in adult patients with R/R T-ALL/LBL. Remission is expected to be short-lived, and the pursuit of disease eradication mandates prompt HSCT bridging. Nonetheless, transplant-related toxicities and post-transplant relapse still represent an extremely relevant mortality burden for this patient population and require careful consideration and mitigation strategies. The NCE regimen was generally safe and manageable. None of the patients experienced neurotoxicity events.

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