VENETOCLAX WITH CHEMOTHERAPY IN CONSOLIDATION IN FIRST LINE THERAPY T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA WITH MRD PERSISTENCE: DATA RALL-2016M STUDY

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INTRODUCTION

MRD persistence after induction is the main factor of poor prognosis for Ph-negative ALL. Blinatumomab was approved for treatment in 1CR with MRD-persistence or in consolidation with MRD-negative status for BCP-ALL. A growing number of publications suggest that venetoclax-containing regimens can achieve deep responses in ETP-ALL and T-ALL patients.

A modified protocol, RALL-2016m, was developed that included targeted drugs venetoclax in the treatment regimen, the use of which is aimed at a more rapid reduction of the residual chemoresistant tumor clone for T-ALL patients.

AIM

To evaluate the results of a study according to the RALL-2016m (NCT06237192) protocol for adult patients with T-cell acute lymphoblastic leukemia.

METHOD

From 2016 Dec to 2026 Apr, 22 new Ph-negative T-ALL patients were treated according to RALL–2016m protocol (ClinicalTrials.gov; NCT03462095) in National Medical Research center for Hematology.

The main features of this protocol:

1. patients with ETP T-ALL received venetoclax 400 mg per day with chemotherapy by protocol from prophase until allo-HSCT. This group of patients was indicated to perform allo-HSCT in the first of 6th months of treatment after achieving MRD-negative CR;
2. patients with MRD persistence in complete remission (CR) on the 70th day by protocol (after second induction) were treated by one cycle of the venetoclax therapy in combination with chemotherapy (56 days 400 mg per day against the background of continued consolidation I, II, III) in T-ALL/LBL.

The median age of T-ALL patients recruited into RALL-2016m (n=32) was 32 years (18-49), f/m 12/20. Under the protocol, TI was diagnosed in 19% (n=6), TII- 41%(n=13), TIII – 38%(n=12), TIV- 2% (n=1). Cytogenetic studies and centralized assessment of minimal residual disease (MRD) by flow cytometry on protocol day +70 (after completion of two induction phases) were performed in all patients. Allogeneic hematopoietic stem cell transplantation was performed in 5 (16%) patients (5 ETP in CR1).

Statistical data processing was carried out using SAS.

CONCLUSIONS

The RALL-2016m study demonstrates the high effectiveness of therapy aimed at rapid reduction of the residual tumor clone. Venetoclax with chemotherapy in consolidation could improve efficacy of therapy in MRD-positive T-ALL.

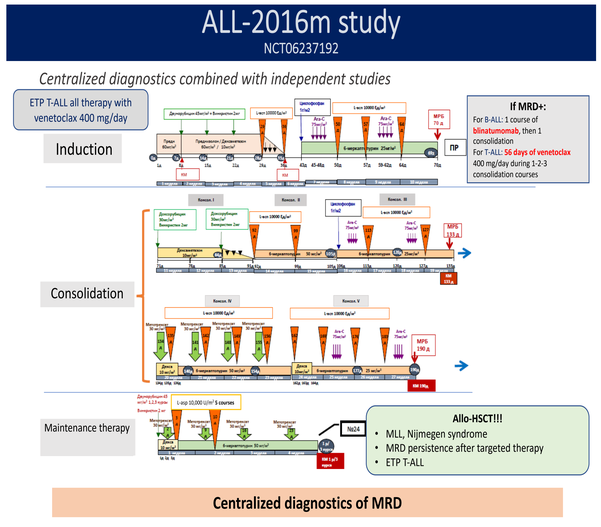
Complete remission was achieved in 100% patients. NO death on the therapy detected.

3-y overall survival and disease-free survival were 79% and 75%. Of the 26 patients (with MRD status), who achieved remission on day 70 of the protocol (end of induction), 8 (31%) patients had persistent MRD.

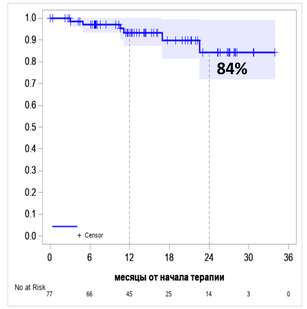
All 8 patients achieved MRD-negative status after venetoclax+chemo cycle.

No patients with the ETP variant had persistent MRD at day 70 (all patients received venetoclax from the start of the therapy).

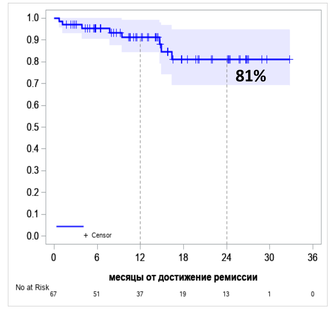
In T-ALL patients according to MRD persistence on day 70: 36-month OS was 40% vs 94% with p<0,0077 (MRD-pos vs MRD-neg), and DFS was 63% vs 76% with p<0,5903 (MRD-pos vs MRD-neg).

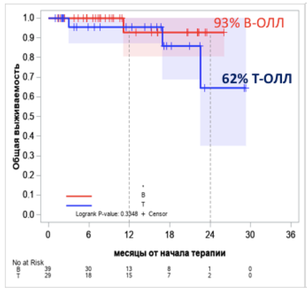


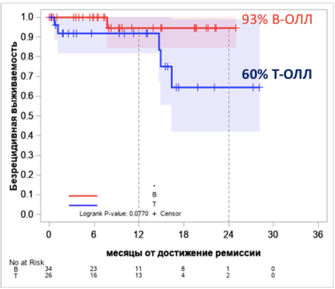
Overall survival



Disease-free survival







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