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THERAPY OF AGGRESSIVE B-CELL LYMPHOMAS WITH TP53 GENE MUTATION

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INTRODUCTION

TP53 gene mutations (mutTP53) in ABL lead to chemoresistance and tumor progression. Retrospective studies demonstrate unsatisfactory results of standard R-CHOP program. The prognostic value of mutTP53 for ABL patients receiving intensive CT is still underinvestigated.

AIM

To evaluate the effectiveness of the R-mNHL-BFM-90 program in the treatment of mutTP53 ABL.

METHOD

119 ABL patients were included: DLBCL - 55, HGL -2, DHL/THL - 13, LB - 11, PML - 21, PBL - 3, FL3A/B - 14. Median age was 44 (18-88) years; M/W=62/57; IPI >2 in 66 (56%); bone marrow lesion in 10 (8%); multiple extranodal foci in 40 (33%). TP53 gene mutations were evaluated by next generation sequencing or Sanger sequencing.

RESULTS

Mut*TP53* were found in 29 of patients (24%): in DLBCL - 14(25%) cases, HGL - 1(50%), DHL/THL - 2(15%), LB - 6(55%), PML - 4(19%), PBL - 1(33%), FL3A/B - 1(7%). Deletion of 17 chromosome (del17p) was detected in 9 (23%) of the 39 cases analyzed. In 8 (89%) cases, del17p was combined with mut*TP53*.

In the mut*TP53* group, 24(83%) received R-mNHL-BFM-90 therapy,11(46%) in combination with targeted therapy. Relapse/progression (R/P) was noted for 11(37%). Complete remission was achieved in 4 patients (CAR-T - 2, allo-HSCT - 1, BCMA - 1), partial remission in 1(CAR-T); stabilization in 2 (palliative therapy); death from other diseases - 4. In 90 wt*TP53* patients 83 (92%) received R-mNHL-BFM-90 therapy, 42 of them (51%) - with targeted therapy. Relapse/progression (R/P) was noted for 11 (12%). Complete remission was achieved in 5 patients (CAR-T - 2, allo-HSCT - 1, CT-2), partial remission in 3 (PCT), death from other diseases – 3.

In mut*TP53* group 3-y OS was 81% vs 95% in wt*TP53* group (p=0.0242); 3-y ES was 59% vs 86%(p=0.0004), median follow-up was 24 (2-68) months (Figure 1).

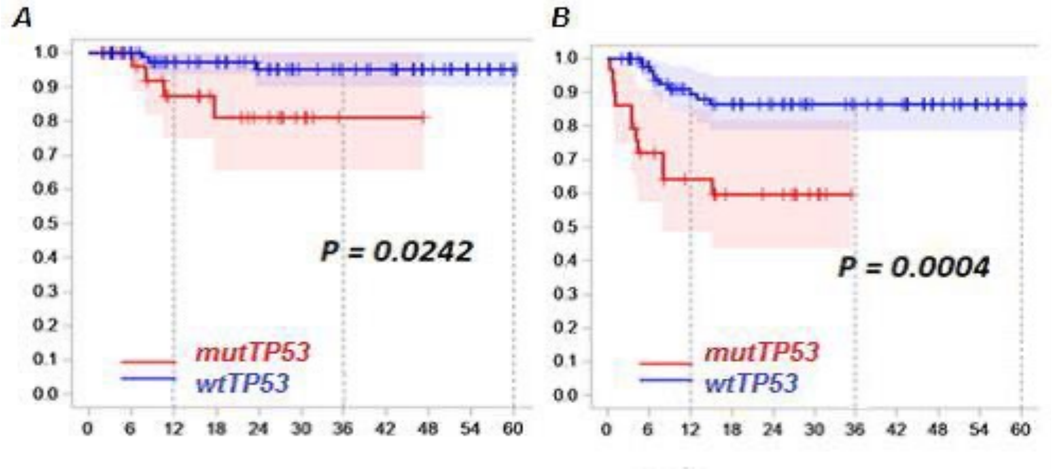


Figure 1. 3-year overall (A) and event free (B) survival in ABL patients with or without TP53 mutations.

CONCLUSIONS

R-mNHL-BFM-90 program improves the results of treatment for ABL patients with mut*TP53*. One can speculate that mitotic catastrophe, caused by intensive multicomponent CT, provoke irreversible changes, which might overcome TP53-mediated chemoresistance. Intensive CT in combination with modern cell therapy (CART,BCMA, allo-HSCT) should determine the treatment success in this patients.

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