Abstract: PB2101

Title: INTENSIVE THERAPY OF AGGRESSIVE B-CELL LYMPHOMAS WITH TP53 GENE MUTATION

Abstract Type: Publication Only

Topic: Aggressive Non-Hodgkin lymphoma - Clinical

Background:

Mutations in the TP53 gene (mutTP53) in aggressive B-cell lymphomas (ABL) are detected with a frequency of 20-36%, lead to chemoresistance and tumor progression. Retrospective studies clearly demonstrate unsatisfactory results of standard (R-CHOP/CHOP-like) therapy programs. The indicators of overall (OS) and event free survival (ES) in the mutTP53 group are significantly lower compared with the group without mutations (wtTP53) ($p < 0.001$). The median ES in mutTP53 group is 9 months . The prognostic value of mutTP53 for ABL patients receiving intensive CT is still underinvestigated; appropriate data are limited and contradictory due to the heterogeneity of the types of therapy and groups analyzed.

Aims:

To evaluate the frequency of mutTP53 in patients with ABL and the effectiveness of the R-mNHL-BFM-90 program in the treatment of these patients.

Methods:

From 2015 to 2023, 119 ABL patiens were included in the study: 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:

TP53 gene mutations 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 (del 17p) was detected in 9 (23%) of the 39 cases analyzed. In 8 out of 9 (89%) cases, del17p was combined with mutTP53. In patients with mutTP53 more cases with IPI >2 (65% vs. 52%) were noted compared to wtTP53.

In the group of mutTP53 patients, 24 of 29 (83%) received R-mNHL-BFM-90 therapy, 11 of them (46%) in combination with targeted therapy. Relapse/progression (R/P) was noted for 11 (37%). As a result of subsequent therapy, 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 wtTP53 patients 83 (92%) received R-mNHL-BFM-90 therapy, 42 of them (51%) in combination 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.

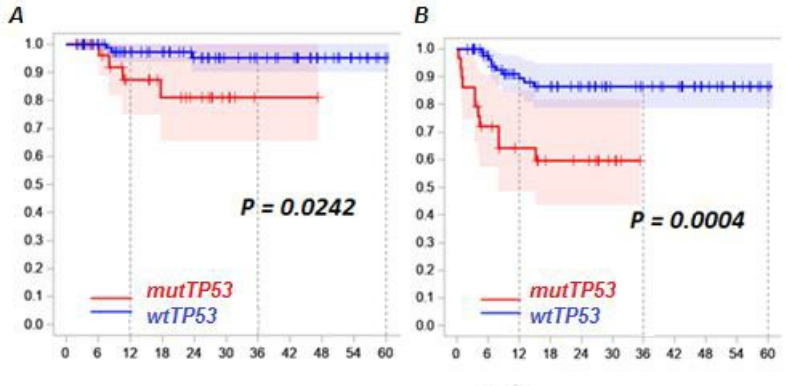
In mutTP53 group 3-year OS was 81% versus 95% in wtTP53 group ($p=0.0242$); 3-year ES was 59% versus 86% ($p=0.0004$), median follow-up was 24 (2-68) months (Figure 1).

Summary/Conclusion:

R-mNHL-BFM-90 program, improves the results of treatment for ABL patients with mutTP53 in comparison with the historical control as a result of therapy intensification. One can speculate that mitotic catastrophe, caused by intensive multicomponent CT, provoke irreversible changes, which in some cases might facilitate overcoming TP53-mediated chemoresistance. To identify a group of ABL patients with an extremely unfavorable prognosis, it is necessary to determine and carefully analyze the spectrum of TP53 mutations on a

larger sample of patients. Setting up clear indications and timing for intensive CT in combination with modern cell therapy (CAR-T, BCMA, allo-HSCT) should determine the treatment success in this group of patients.

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



Keywords: High-grade non-Hodgkins-lymphoma, p53, Diffuse large B cell lymphoma, Burkitt's lymphoma