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OUTCOMES OF *BCL2-R+* AND *BCL2-R-* FOLLICULAR LYMPHOMA TREATMENT

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INTRODUCTION

About 80% of patients with FL have an indolent course of the disease, 20% have an aggressive course such as DLBCL. Every fifth patient with an indolent course after first-line therapy has POD24. According to the new WHO classification of haematolymphoid tumors, FL must be divided into classic and non-classic FL. There are few reports that indicate the pathogenetic differences between *BCL2-R+* FL and *BCL2-R-* FL, which underlie tumor heterogeneity.

AIM

Determine the effect of *BCL2* gene rearrangement on the prognosis of FL and evaluate the effectiveness of treatment in compared groups (*BCL2-R+/-)* of patients (pts), and analyze cases of treatment failure.

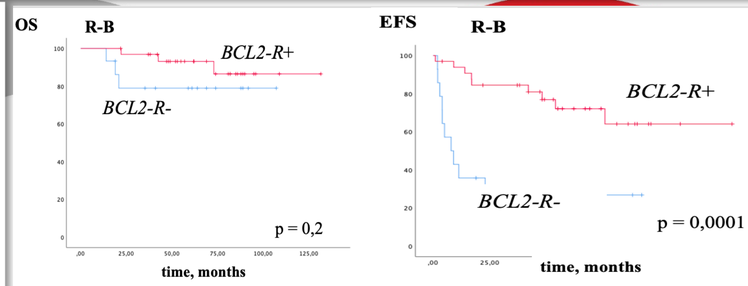
METHOD

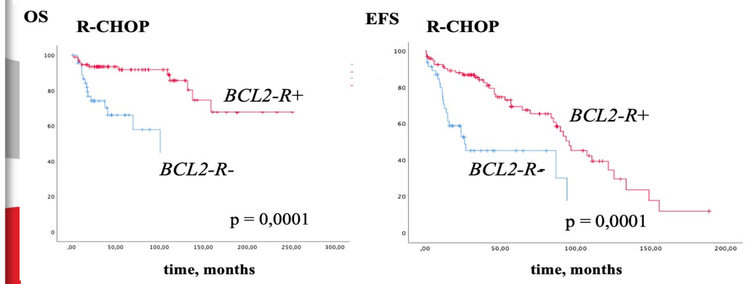
A retrospective-prospective study (2001-2022) at the National Medical Research Center for Hematology of the Russian Ministry of Health (Moscow) included 362 pts with grade 1-3A FL before treatment. Cytogenetic research was performed in 265/362(73%) cases. *BCL2* gene rearrangement was determined by karyotyping or FISH.

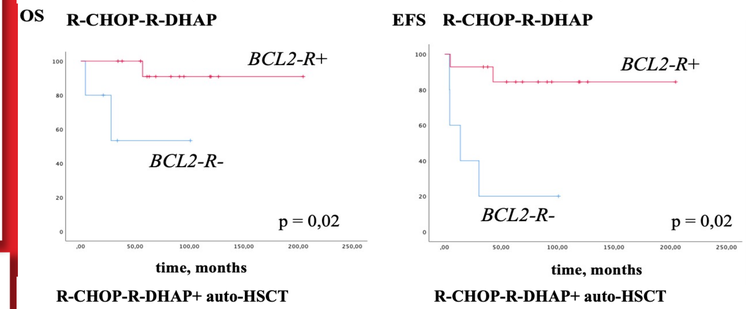
RESULTS

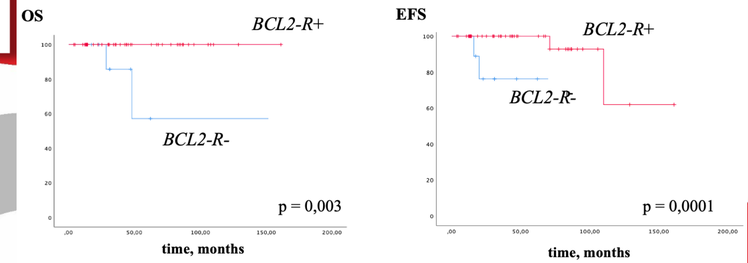
Five-year, 10-year and 20-year OS rates of 362 pts with FL on all lines of therapy were 88%, 76% and 58%, respectively. Five-year, 10-year and 20-year EFS of 362 pts with FL on all lines of therapy were 68%, 45% and 20%, respectively. Median follow-up 92 (1-251) months. After cytogenetic analysis, two groups of pts were formed: a group with the presence of *BCL2* gene rearrangement (*BCL2-R+*, n=196/362(54%)) and a group with the absence of *BCL2* gene rearrangement (*BCL2-R-*, n=69/362(19%)). The group without cytogenetic testing (n=97/362(27%) was excluded from the analysis. The *BCL2-R+/-* FL groups were comparable in demographic and clinical parameters. In the *BCL2-R-* FL group, grade 3A predominated (p=0.003) and Ki67>35% (p=0.001), and bone marrow involvement was less common (p=0.002). The *BCL2-R+* FL group without risk factors (short history, bulky, 3A grade and Ki67>35%) was chemosensitive to R-B and R-CHOP regimens, with risk factors it was chemosensitive to cisplatin-containing regimens and auto-HSCT in the first line therapy. The effectiveness of therapy in terms of OS and EFS was 85-100%, respectively (p=0.0001). In the *BCL2-R-* FL group, without dependence on prognostic factors, there were early relapses/progressions (POD24) on standard and high-dose therapy (p=0.0001). EFS of pts did not exceed 60% (p=0.0001) with standard regimens, and 75% (p=0.0001) with auto-HSCT in the first remission.

	BCL2-R+	n=196	*BCL2-R-*	n=69
R-CHOP-R-DHAP-аутоТСКК	48	24%	9	13%
R-CHOP-R-DHAP	14	7%	5	7%
R-CHOP	97	50%	44	64%
R-B	37	19%	11	16%









CONCLUSIONS

The *BCL2-R+* FL group is a favorable option compared to *BCL2-R-* FL, where a risk-adapted approach to therapy is important. *BCL2-R-* FL is a prognostically unfavorable variant, where 40% of pts develop early relapses/progression on standard treatment regimens and 30% when using high-dose therapy +/- auto-HSCT. The study results indicate the need for fundamentally new approaches to therapy.



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