Preliminary outcomes of treatment in young B-CLL patients with poor prognostic indicators, utilizing the FCR regimen combined with ibrutinib and venetoclax in a fixed-duration protocol

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INTRODUCTION

Traditional approaches to the treatment of young patients with B-CLL, depending on the biological characteristics of tumor, include FCR or various combinations of targeted agents. Data on their combined use are limited. The experience with FCR regimen combined with ibrutinib (iFCR) in a fixed-duration regimen has demonstrated high rates of MRD-negative remission in young patients with B-CLL with various biological features of the tumor [I.E. Ahn, 2024]. The combination of BTK and BCL2 inhibitors exhibits synergistic effects and, in some cases, leads to rapid tumor clearance. However, no data on the FCR regimen combined with BTK and BCL2 inhibitors presented so far up to our knowledge.

AIM

The aim of the study was to present the first experience of using FCR regimen combined with ibrutinib and venetoclax in a fixed-duration regimen in young B-CLL patients with unfavorable prognostic factors

METHOD

In the period from 2024 to 2026, 6 patients with B-CLL were included in the study, average age = 54 (42 – 65) years. Distribution by stages according to Rai – stage I (n = 3), II (n = 2), IV (n = 1), according to Binet – stage B (n = 5), stage C (n = 1). The average leukocyte count was 60 (22 – 147) x 10*9/l. The average SUVmax value according to 18f-FDG PET/CT data was 4.37 (1.89 – 7.7). The following UPF were detected: unmutated variant of IGVH genes (100%, n = 6), mutation in the SF3B1 gene in combination with deletion of 11q22/ATM (33%, n = 2), mutation in the NOTCH1 gene (17%, n = 1), trisomy 12 (33%, n = 2). Deletions of 17p13/mutations in the TP53 gene were not detected.

CONCLUSIONS

We conclude FCR regimen with ibrutinib and venetoclax facilitates the achievement of MRD-negative remission in 60% of patients after just 2 cycles of therapy. Conducting only four courses of chemotherapy and using targeted therapy in a stop-therapy regimen will likely reduce the incidence of infectious and hematological complications. The "stop-therapy" concept represents the most advantageous strategy, being both cost-effective and preserving antitumor sensitivity in the event of a relapse of the disease. To draw definitive conclusions, longer follow-up periods and a larger number of patients are needed. To determine the optimal timing for CAR-T cell therapy, continued studies assessing immune status are promising.

RESULTS

All 6 patients received a pre-treatment regimen of dexamethasone and cyclophosphamide with the addition of ibrutinib at a dose of 280 mg/day for 3-5 days. The first course of chemotherapy was administered using the FCR regimen with ibrutinib at a dose of 420 mg/day for 10 days, with the addition of venetoclax starting on day 5, with a gradual dose escalation from 50 to 200 mg/day. Beginning with the second cycle, treatment was administered using the FCR regimen with ibrutinib at a dose of 420 mg/day and venetoclax at a dose of 400 mg/day for 10 days of each cycle. No severe toxic or infectious complications were observed. All 6 patients completed therapy.

After each cycle of therapy, MRD was assessed: all 6 patients achieved MRD negativity at the end of therapy (including 4/6 (67%) patients after 2 cycles for peripheral blood and after 3 cycles for bone marrow). PET-negative remission was also achieved in all 6 patients (100%) after the end of therapy.

Three patients underwent T-cell assessment after completion of therapy. Complete immune reconstitution was observed in the one patient 10 months after completion of treatment.

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