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Management Challenges in Patients With Treatment-Free Remission of Chronic Myeloid Leukemia

Vasile Musteata MD, PhD, MPH[1,2]
[1]N. Testemitanu State University of Medicine and Pharmacy, Chisinau, Republic of Moldova
[2]Institute of Oncology, Chisinau, Republic of Moldova

INTRODUCTION

Tyrosine kinase inhibitors (TKIs) discontinuation in patients with treatment-free remission (TFR) of chronic myeloid leukemia (CML) remains challenging and is associated with the ambiguous results related to the withdrawal effects and unstable hematological and molecular responses.

AIM

The assessment of the short- and long-term results of treatment discontinuation in CML patients with deep molecular responses (DMRs).

METHOD

Design: We performed an observational and cohort study. The diagnosis was determined on the basis of WHO and European LeukemiaNet criteria. The patients' follow-up was related to the hospitalized and outpatient care.
This prospective, cohort study included 25 patients with chronic phase of CML, treated at the Oncologic Institute from Moldova between 2017 and 2023. The age range was 29 to 73 years (average age: 46.5 years). The male/female ratio was 1:1.5.
Interventions: The quantitative reverse transcription polymerase chain reaction (PCR) was performed to determine the expression of the BCR-ABL p210 and p190 transcripts. Antineoplastic regimens used were single-agent therapies with different generations of TKIs. Descriptive statistics and big data analytics were applied.
Outcomes Evaluation: The results of treatment were estimated by complete hematological response, DMR, and their span.

RESULTS

In 12 (48%) cases, the initial rate of BCR-ABL p210-positive cells was less than 50%. Only 2 (8.0%) patients proved to be positive for BCR-ABL p190 transcript. DMRs were obtained in 18 (72.0%) patients after imatinib therapy and in 7 (28.0%) patients after therapy with 2nd TKIs generation. The molecular relapses occurred in 7 (28.0%) patients. All patients with molecular relapses had the initial BCR-ABL p210 transcript expression >50%. The complete molecular responses (CMRs) ranged between 2.5 and 26 months before TKIs discontinuation. Its average value (35.8 months) was much shorter ($P<0.05$) than in patients without molecular relapses (56.4 months). The range of BCR-ABL p210 transcript in the relapsed cases was 0.002% to 1.16%. These patients attained the 2nd CMR after resuming TKIs treatment at a higher dosage or generation.

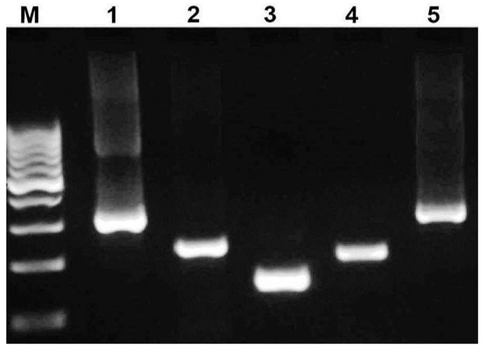


Figure 1. RT-qPCR: BCR-ABL p210 transcript

Presence of molecular relapse in CML patients	Number of patients		Gender				Duration of complete molecular response before the treatment discontinuation, months	Generation of TKIs, which induced complete molecular response before relapse				Duration of complete molecular response after the treatment discontinuation, months	Initial expression of BCR/ABL gene transcripts before treatment with TKIs,%	Expression of BCR/ABL gene transcripts after discontinuation of treatment with TKIs,%	ECOG-WHO score
			Males		Females			I		II					
	No	%	No	%	No	%		No	%	No	%				
Withoutmolecular relapse	16	69.6	8	34.8	8	34.8	18.5-115	11	68.8	5	31.2	6-12	<50	0	0-1
With molecular relapse	7	30.4	2	8.7	5	21.7	6-26	4	57.1	3	42.9	2.5-26	>50	0.002–0.56	0-1

Table 1. Clinical and biological profile of CML patients with CMR and TKIs treatment discontinuation

CONCLUSIONS

TKIs discontinuation and TFR option may be considered as a justifiable management approach to CML patients of male gender, with chronic phase, long-lasting DMR, low BCR-ABL p210 transcript expression, and absence of BCR-ABL p190 transcript at diagnosis.

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CONTACT INFORMATION

Vasile Musteata, associate professor, MPH,
vasile.musteata@usmf.md