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Structure of Chronic Myeloleukemia Patients in Uzbekistan: Analysis and Perspectives

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Abstract The aim of the study was to systematize, structure and present information on the age and sex structure of chronic myeloleukemia (CML) patients and the long-term results of therapy with tyrosine kinase inhibitors (TKIs). The study enrolled 1033 patients diagnosed with CML who were treated with tyrosine kinase inhibitors of first generation (Glivec (imatinib) and 42 patients who were treated with the second generation (Tasigna (nilotinib)) from different regions of Uzbekistan. The carried out work will allow to replenish the register with the obtained data, and the analysis of patients' structure. Also this study to form and develop the register of patients with CML and oncohematological patients in general.

Keywords Chronic myeloleukemia (CML), Tyrosine kinase inhibitors (TKIs), Glivec, Tasigna, Sex and age, Regional, Registry

1. Introduction

The use of tyrosine kinase inhibitors (TKIs) in the treatment of chronic myeloleukemia (CML) patients has increased the survival rate [1-5]. Sufficiently long history of TKIs use in Uzbekistan allows us to make certain observations and conclusions about the effectiveness and long-term effects of the therapy, which raises the question of the need to streamline the data accumulated over a long period of time. The creation of a registry of patients with CML who have been treated with TKIS will allow further improvement of treatment protocols and their effectiveness [8-13].

2. Main Body

2.1. The Purpose of Our Research

To systematize, structure and present information on the sex and age structure of patients with CML and the long-term results of therapy with tyrosine kinase inhibitors (TKIs).

2.2. Material and Methods of Study

The study included 1033 patients with established diagnosis of CML who received first generation (Glivec (imatinib)) tyrosine kinase inhibitors and 42 patients who received second generation (Tasigna (nilotinib)) drugs from different regions of the Republic of Uzbekistan. Patients with the presence of Philadelphia chromosome (Ph+) and/or the presence of BCR-ABL transcript confirmed by cytogenetic method were selected for the study [7].

We studied the structure of patients, their distribution by sex and age. A subgroup of patients with CML treated with Glivec included 991 patients, of whom 520 were men and 471 women. Another part of patients with CML received the second-generation TKIs - Tasigna. The subgroup of patients with CML treated with "Tasigna" included 42 patients, including 24 men and 18 women. Retrospective studies of treatment efficacy were performed.

Statistical processing was performed using an online calculator [14].

2.3. Results of the Study

The sex and age structure of the groups of patients treated with the first (Glivec) and second (Tasigna) generations of TKIs drugs was studied (Fig. 1-2; Table 1-2).

As we can see from Figure 1, patients of the middle age category prevailed among the patients. The largest proportion were patients from 30 to 45 and 46 to 60 years old. The data presented in the table indicate the absence of statistically significant differences between male and female patients in all age categories studied among the patients who took Glivec.

There was also a study of the gender and age structure of the group of patients who received the second generation TKIs drug - "Tasigna" (Fig. 2; Table 2). In the course of the study, no statistically significant differences were found in the group of patients with CML who took Tasigna. In the age structure of patients who received "Tasigna", patients

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aged 30-45 and 46-60 years prevailed (table 2).

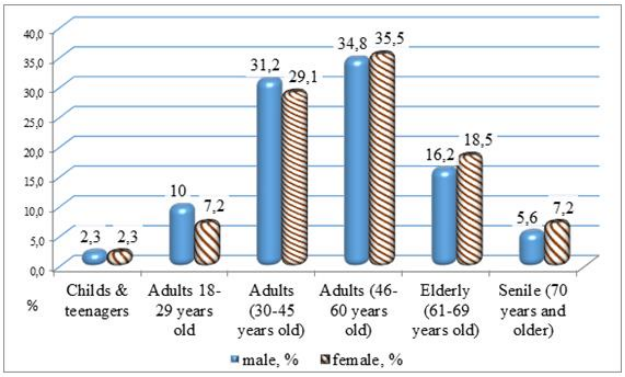

Figure 1. Gender and age structure among patients treated with "Glivec"

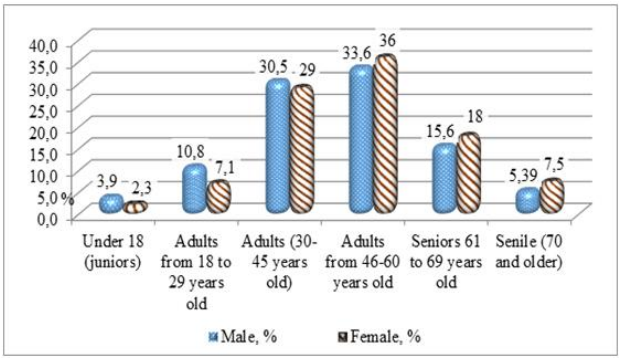

Figure 2. Age and sex structure among patients who received "Tasigna"

The distribution of patients by region was also studied. Patients from the regions were represented in different proportions among patients who received Glivec. Thus, the largest proportion of patients were from Samarkand - 11.0%, from Khorezm – 9.2%, from Tashkent city and Tashkent region - 8.8% and 8.9% each, Kashkadarya - 8.4%, Namangan and Andijan cities - 8.0% and Surkhandarya - 7.7%.

The average rates in the regional structure of the examined group of oncohematological patients were observed in Bukhara province - 6.6%, in the Republic of Karakalpakstan - 6.1%, in Ferghana province - 5.8%, in Navoi city - 4.4% and in Jizzakh - 3.3%.

Patients from Syrdarya province – 2.6%, and from Kashkadarya province - 1.1% and Namangan province - 0.2% were the least observed. At the same time in the two latter there is a sharp gap between Kashkadarya city and Kashkadarya region, as in the case of Namangan city and Namangan region, which is related to the population's addressing to large regional clinical-diagnostic centers.

The comparison of the regions where CML patients were admitted showed statistically significant differences between Tashkent city and Bukhara region (χ^2=4.79; OR=1.39; 95% CI: 1.00-1.94) as well as the comparison of Tashkent city with other regions and region centers: Jizzak (χ^2=26.6; OR=2.83; 95% CI: 1.88-4.26), Navoi region (χ^2=15.7; OR=2.10; 95% CI: 1.44-3.05), the Republic of Karakalpakstan (χ^2=5.73; OR=1.51; 95% CI: 1.08-2.13), Samarkand region (χ^2=2.72; OR=0.78; 95%DI(CI): 0.58-1.05), Syrdarya region (χ^2=35.8; OR=3.62; 95%DI(CI): 2.31-5.66), Fergana region (χ^2=7.15; OR=1.60; 95%DI(CI):1.13-2.26).

Table 1. Differences in sex and age structure among patients with CML treated with Glivec

	Groups		χ^2	RR	95%CI	OR	95%CI:
	Age	Other					
under 18 years old							
Male	12 (2.3%)	508 (97.7%)	0.001	0.99	0.44- 2.22	0.99	0.43- 2.26
Fe- male	11 (2.3%)	460 (97.7%)					
18 to 29 years old							
Male	52 (10.0%)	468 (90.0%)	2.41*	1.17	0.98- 1.40	1.43	0.91- 2.24
Fe- male	34 (7.2%)	437 (92.8%)					
30-45 years old							
Male	162 (31.2%)	358 (68.8%)	0.50	1.05	0.92- 1.19	1.10	0.84- 1.45
Fe- male	137 (29.1%)	334 (70.9%)					
46-60 years old							
Male	181 (34.8%)	339 (65.2%)	0.046	0.99	0.87- 1.12	0.97	0.75- 1.26
Fe- male	167 (35.5%)	304 (64.5%)					
61-69 years old							
Male	84 (16.2%)	436 (83.8%)	0.93	0.92	0.78- 1.09	0.85	0.61- 1.18
Fe- male	87 (18.5%)	384 (81.5%)					
70 years and older							
Male	29 (5.6%)	491 (94.4%)	1.12	0.87	0.66- 1.14	-	0.46- 1.27
Fe- male	34 (7.2%)	437 (92.8%)					

Table 2. Distribution by sex and age of patients with CML who received Tasigna

	Groups		χ^2	RR	95%CI	OR	95%CI:
	Age	Other					
under 18 years old							
Male	2(8.3%)	22 (91.7%)	1.58	1.82	1.37- 2.41	-	-
Fe- male	0(0%)	18 (100%)					
18 to 29 years old							
Male	2(8.3%)	22 (91.7%)	0.09	0.86	0.31- 2.39	0.73	0.09-5.72
Fe- male	2(11.1%)	16(12.5%)					
30-45 years old							
Male	8(33%)	16 (72.7%)	0.54	0.81	0.46- 1.45	0.63	0.18-2.20
Fe- male	8(44.4%)	10 (55.5%)					
46-60 years old							
Male	9 (38%)	15(62.5%)	1.12	1.34	0.81- 2.22	2.10	0.53-8.39
Fe- male	4 (22.2%)	14(77.8%)					
61-69 years old							
Male	2 (8.3%)	22(91.7%)	0.68	0.67	0.22- 2.03	0.46	0.07-3.06
Fe- male	3(16.7%)	15(83.3%)					
70 years and older							
Male	1 (4.2%)	23(95.8%)	0.04	0.87	0.21- 3.57	0.74	0.04-12.67
Fe- male	1 (5.6%)	17(94.4%)					

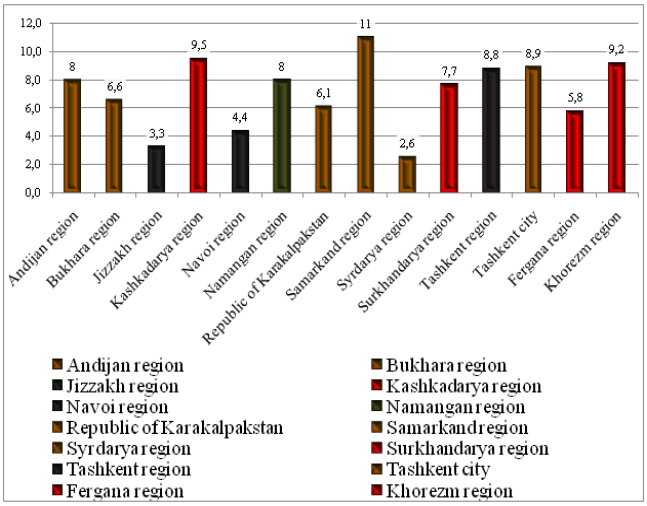

Figure 3. Structure by regions (regions) of patients who received Glivec

A similar picture in terms of the regional structure of the study group was observed among the 42 patients who received the more modern second-generation TKIs drug, Tasigna. The largest number of patients – from Tashkent city, followed by Tashkent, Fergana, Bukhara, Navoyi regions and the Republic of Karakalpakstan - 9.5% each. Samarkand, Surkhandarya and Khorezm provinces had a slightly lower percentage of patients with CML - 7.1% each. Patients from Kashkadarya and Syrdarya provinces were detected less frequently among the patients of this group - 4.8% and significantly less frequently in 2.4% of cases from Namangan province (Fig. 4).

Statistically significant differences were found between the number of patients from Tashkent city where more patients were admitted than from Namangan region (χ^2=6.1 ; OR=9.6; 95% CI: 1.15-81.02) (Table 4).

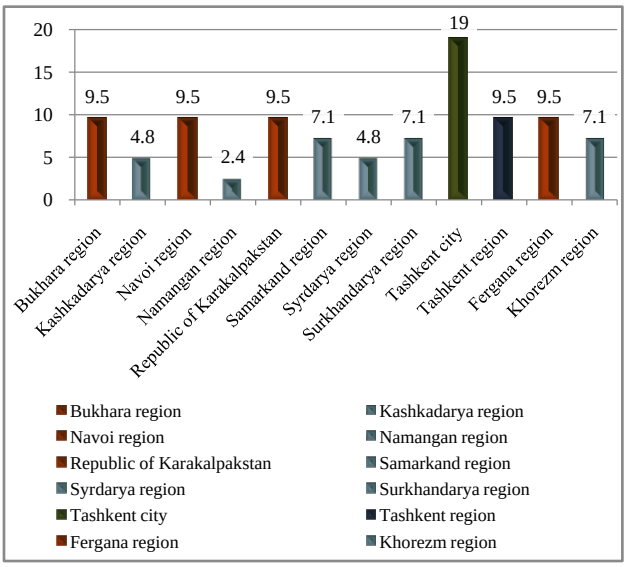

Figure 4. Structure by region among patients with CML who received Tasigna

There was also a marked trend in the differences in the number of patients admitted from Tashkent city and from Kashkadarya and Syrdarya regions, which can be explained by the interregional migration of patients and their families to the more developed from the point of view of health care in the large metropolitan center.

The most pronounced differences in the distribution of patients with CML patients treated with Tasigna were observed between Tashkent city and Kashkadarya region

(χ2=4.1; OR=4.71; 95% CI: 0.94-23.67), where there was a pronounced tendency for the prevalence in the capital. The degree of detection of this category of patients was also significantly higher in Tashkent city compared to Namangan region (χ2=6.1; OR=9.6; 95% DI(CI): 1.15-81.02).

Of the total number of patients with CML (n=1,033), 180 patients were resistant to the therapy.

78 of them received TKIs drugs (Glivec and Tasigna).

Table 3. Differences in prevalence by oblast among patients with CML treated with Glivec

	Groups				χ^2	OR	95%CI:
	In the region		Others				
	Abc	%	Abc	%			
Andijan region							
Tashkent	88	8.9	903	91,1	0.53	1.13	0.82-1.55
Andijan	79	8	912	92,0			
Bukhara region							
Tashkent	88	8.9	903	91,1	**4.79**	**1.39**	**1.00-1.94**
Bukhara	65	6.6	926	93,4			
Jizzakh region							
Tashkent	88	8.9	903	91,1	**26.6**	**2.83**	**1.88-4.26**
Jizzakh	33	3,3	958	96,7			
Kashkadarya region							
Tashkent	88	8.9	903	91,1	0.22	0.93	0.69-1.26
Kashkadarya	94	9,5	897	90,5			
Navoi region							
Tashkent	88	8.9	903	91,1	**15.7**	**2.10**	**1.44-3.05**
Navoi	44	4,4	947	95,6			
Namangan region							
Tashkent	88	8.9	903	91,1	0.32	1.10	0.80-1.50
Namangan	81	8	910	92,0			
Republic of Karakalpakstan							
Tashkent	88	8.9	903	91,1	**5.73**	**1.51**	**1.08-2.13**
Karakalpakstan	60	6,1	931	93,9			
Samarkand region							
Tashkent	88	8.9	903	91,1	**2.72**	**0.78**	**0.58-1.05**
Samarkand	110	11	881	88,9			
Syrdarya region							
Tashkent	88	8.9	903	91,1	**35.8**	**3.62**	**2.31-5.66**
Syrdarya	26	2,6	965	97,4			
Surkhandarya region							
Tashkent	88	8.9	903	91,1	0.96	1.173	0.85-1.62
Surkhandarya	76	7,7	915	92,3			
Tashkent region							
City	88	8.9	903	91,1	0.006	1.01	0.74-1.38
Region	87	8,8	904	91,2			
Fergana region							
Tashkent	88	8.9	903	91,1	**7.15**	**1.60**	**1.13-2.26**
Fergana	57	5,8	934	94,2			
Khorezm region							
Tashkent	88	8.9	903	91,1	0.06	0.96	0.71-1.31
Khorezm	91	9,2	900	90,8			

Table 4. Distribution by sex and age of patients with CML who received Tasigna

	Groups				χ^2	OR	95%CI:
	In the region		Others				
	Abc	%	Abc	%			
Bukhara region							
Tashkent	8	19	34	80.9	1.6	2.24	0.62-8.09
Bukhara	4	9,5	38	90.5			
Kashkadarya region							
Tashkent	8	19	34	80.9	**4.1**	**4.71**	**0.94-23.67**
Kashkadarya	2	4,8	40	95.2			
Navoi region							
Tashkent	8	19	34	80.9	1.6	2.24	0.62-8.09
Navoi	4	9,5	38	90.5			
Namangan region							
Tashkent	8	19	34	80.9	**6.1**	**9.6**	**1.15-81.02**
Namangan	1	2,4	41	97.6*****			
Republic of Karakalpakstan							
Tashkent	8	19	34	80.9	1.6	2.2	0.62-8.09
Karakalpakstan	4	9,5	38	90.5			
Samarkand region							
Tashkent	8	19	34	80.9	2.	3.1	0.75-12.46
Samarkand	3	7,1	39	92.8			
Syrdarya region							
Tashkent	8	19	34	80.9	**4.1**	**4.7**	**0.93-23.67**
Syrdarya	2	4,8	40	95.2			
Surkhandarya region							
Tashkent	8	19	34	80.9	2.6	3.1	0.75-12.46
Surkhandarya	3	7,1	39	92.8			
Tashkent region							
City	8	19	34	80.9	1.6	2.2	0.62-8.09
Region	4	9,5	38	90.5			
Fergana region							
Tashkent	8	19	34	80.9	1.6	2.2	0.62-8.09
Fergana	4	9,5	38	90.5			
Khorezm region							
Tashkent	8	19	34	80.9	2.6	3.1	0.75-12.46
Khorezm	3	7,1	38	90.5			

As a result, of therapy with TKIs drugs, resistance developed in 78 patients. And in 56 cases the cause of resistance development was the TKIs drugs themselves, i.e. "Glivec" and "Tasigna". At the same time in 47 patients were fixed violations in the scheme of drugs intake and in 9 patients drug intolerance was observed. In the remaining 18 cases, medication errors were noted.

Of the 78 therapy-resistant oncohematological patients, 8 could be categorized as "young" age, i.e., 19 to 29 years old, 27 as "mature" age, 30 to 44 years old, and 42 over 45 years old.

3. Conclusions

The conducted work will allow to replenish the register with the data obtained, and the analysis of the structure of patients will allow to expand the understanding of the structure of patients, to give a full assessment of the long-term results of treatment of this category, to form and develop a register of patients with CML and oncohematological patients in general. The formation of such register and its support at the state level will allow to visualize the structure of the study group, monitor the

effectiveness of CML therapy and improve its efficiency. This is especially relevant, in order to improve the quality and longevity of CML patients, in particular the long-term survival rate [7-9].

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