Sakarya Tıp Dergisi
Sakarya Med J

e-ISSN: 2146-409X
Publisher: Sakarya University

Vol. 15, No. 2, 153-163, 2025
DOI: http://doi.org/10.31832/smj.1630054

Research Article

Long-Term Safety and Efficacy of Imatinib in Chronic Myeloid Leukemia: Real-World Evidence from a Single-Center Study

Nevin Alayvaz Aslan[1*], Özde Elver[2], Kayıhan Kara[1], İsmail Can Kendir[1], Hande Şenol[3], Nil Güler[1]

[1] Pamukkale University Faculty of Medicine, Department of Hematology, Denizli, Türkiye

nevina@pau.edu.tr,
kayihankara@gmail.com,
can_kendir@hotmail.com,
nilvecay@yahoo.com,
ror.org/01etz1309

[2] Aydın Government Hospital, Department of Hematology, Aydın, Türkiye

ozde.elver@gmail.com,

[3] Pamukkale University Faculty of Medicine, Department of Biostatistics, Denizli, Türkiye

handesenol@gmail.com,
ror.org/01etz1309

* Corresponding Author

Received: 07.02.2025
Accepted: 26.05.2025
Available Online: 12.06.2025

Objective: Imatinib mesylate, a tyrosine kinase inhibitor (TKI), has revolutionized CML treatment, improving patient survival to levels comparable to the general population. This study evaluates treatment response, side effects, and survival rates in CML patients followed at our clinic.

Materials and Methods: A retrospective analysis was conducted on 76 CML patients treated with imatinib at Pamukkale University Hospital between August 2000 and April 2022. Treatment responses, side effects, and survival outcomes were assessed.

Results: The median age of patients was 49 years, with 93.4% in the chronic phase and 6.6% in the accelerated phase. Patients achieving MMR at the 6th month had significantly longer event-free survival (EFS) (198.09 ± 12.39 months; p<0.0001). The 10-year overall survival (OS) rate was 94.2%, and the 5-year OS rate was 98.5%. A total of 46.05% of patients were switched to second-generation TKIs due to insufficient response or side effects. Cox regression analysis revealed that older age at diagnosis increased the risk of death, and failure to achieve MMR at the 12th month raised event risk by 76-fold. During treatment, 30.3% of patients experienced imatinib-related side effects, with serious side effects observed in 9.2% of patients.

Conclusion: Imatinib remains a highly effective and well-tolerated treatment for CML in real-world settings. The outcomes observed in this study aligned similarly with those reported in international clinical trials. Achieving early molecular responses significantly improves long-term survival. These findings underscore the importance of adherence to treatment protocols and regular monitoring.

Keywords: Chronic Myeloid Leukemia, Imatinib, Major Molecular Response, Survival

1. INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm characterized by the uncontrolled proliferation of mature and maturing granulocytes. The pathogenesis involves the fusion of the ABL gene, located on the q34 band of chromosome 9, with the BCR gene, located on the 11q band of chromosome 22, forming the BCR-ABL1 fusion gene on chromosome 22 (Philadelphia chromosome).[1] The BCR::ABL1 fusion gene encodes the p210 peptide, which possesses tyrosine kinase activity and drives clonal proliferation. Approximately 85% of patients present in the chronic phase, and if untreated, they may progress to the accelerated phase or blast crisis. Various scoring methods are used to predict the prognosis of patients. The Sokal risk score considers the patient's age, platelet count at diagnosis, percentage of blasts in the peripheral smear, and spleen size palpable below the costal margin.[2] The EUTOS risk score, a more recent method to predict cytogenetic response and progression-free survival (PFS), considers the percentage of basophils in the peripheral smear and spleen size palpable below the costal margin at diagnosis.[3]

The discovery of imatinib mesylate, a BCR::ABL1 tyrosine kinase inhibitor, in 1998 and its approval for the treatment of CML in May 2001 dramatically changed the course of the disease. Before the discovery of imatinib, CML was a fatal disease; today, it is treated as a chronic disease, and the majority of patients achieve a survival rate comparable to that of the general population.[4] In the multicenter Phase 3 IRIS study, the 10-year overall survival (OS) rate with imatinib was found to be 83.3%.[5] Imatinib is the only TKI that is reimbursed for newly diagnosed chronic-phase

Cite as: Surname N, Surname N. Long-Term Safety and Efficacy of Imatinib in Chronic Myeloid Leukemia: Real-World Evidence from a Single-Center Study. *Sakarya Med J.* 2025;15(2):153-163. doi:10.31832/smj.1630054

CML in our country. While generally well-tolerated, imatinib treatment may require switching to second-generation TKIs (2GTKIs) in cases of resistance or insufficient response, loss of response, or side effects. Molecular methods, particularly the measurement of BCR::ABL1 fusion mRNA using reverse transcriptase polymerase chain reaction (RT-PCR), are crucial for monitoring treatment response at regular intervals. [6,7]

This study aims to evaluate the response to imatinib treatment, the development of side effects, and the rates of switching to second-generation TKIs in adult CML patients treated at our center. By doing so, it seeks to address gaps in the current evidence and provide clinically relevant insights.

2. MATERIALS AND METHODS

2.1. Patient population

The study included chronic or accelerated-phase CML patients who were treated with imatinib and followed for at least one year at Pamukkale University Adult Hematology Clinic between August 2000 and April 2022. The diagnosis of CML was established cytogenetically and molecularly by demonstrating the Philadelphia (Ph) chromosome or the BCR::ABL fusion according to the World Health Organization (WHO) diagnostic criteria for myeloid and lymphoid neoplasms.[6,8] Definitions of chronic and accelerated phases were established following the European LeukemiaNet (ELN) recommendations.[9] Risk classification was performed using the Sokal and the European Treatment and Outcome Study for CML (EUTOS) scores.[1,2] Until August 2012, the original imatinib mesylate molecule was used in treatment, after which both generic and original molecules were utilized due to the introduction of generics in our country. Response evaluations (molecular and cytogenetic responses) of patients treated with imatinib were performed according to the ELN guidelines. Patients' demographic and clinical characteristics, Sokal score, EUTOS score, duration of imatinib use, BCR-ABL IS scores at the 6th and 12th months, imatinib-related side effects, and reasons for transitioning to second-generation TKIs were retrospectively analyzed using data from patient files and the hospital's electronic information system. Drug-related side effects were graded according to the Common Terminology for Adverse Events (CTCAE) definitions.[10] This study was conducted under the principles of the Declaration of Helsinki and written informed consent was secured from each patient or their first-degree relatives. Ethical approval was obtained from the Ethics Committee of the Pamukkale University (approval number 14.06.2023-E.380591).

2.2. Survival analysis

Overall survival (OS) was defined as the time from diagnosis to death. Event-free survival (EFS) was defined as survival without progression to accelerated phase or blast crisis, loss of complete hematological response, loss of major cytogenetic response or death from any cause during imatinib treatment.

2.3. Cytogenetic and molecular analysis

For response evaluation, BCR::ABL transcript levels were measured every three months in peripheral blood using quantitative reverse transcription PCR (qRT-PCR) on the international scale (IS), in line with ELN recommendations.[7,11] Absence of Ph-positive metaphases in the bone marrow (0%) or IS <1% was considered a complete cytogenetic response (CCyR), and IS <0.1% was considered a major molecular response (MMR). For patients who achieved MMR, BCR::ABL monitoring was performed every 3–6 months.

2.4. Statistical methods

All statistical analyses were performed using SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)). Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were defined by the mean ± standard deviation and median (IQR: 25th-75th percentiles) while categorical variables were expressed as frequencies and percentages. Shapiro Wilk test was used for the determination of normal distribution. Group comparisons were performed using the chi-square test or Fisher's exact test for categorical variables, and the

Student's t-test or Mann-Whitney U test for continuous variables, depending on the normality of the data.

Survival analyses were conducted to evaluate OS and EFS. Kaplan-Meier survival curves were generated, and differences between groups were compared using the log-rank test. Cox proportional hazards regression analysis was used to identify risk factors affecting survival outcomes. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated to assess the impact of prognostic variables on survival. A p-value <0.05 was considered statistically significant.

3. RESULTS

3.1. Clinical features of the patients

Seventy-six CML patients were included in the study and the median age was 49 ± 12.92 years, with a female-to-male ratio of 42/34. At diagnosis, 93.4% (n=71) of the patients were in the chronic phase, while 6.6% (n=5) were in the accelerated phase of CML. According to the Sokal score, 12 patients (19.67%) were classified as high-risk, while 7 patients (12.28%) were classified as high-risk according to the EUTOS score. A total of 43.4% of patients had at least one comorbidity. Detailed demographic and clinical characteristics of the patients are provided in Table 1.

Table 1.

Characteristics of the patients

		Mean ± SD	*Med (IQR)* *N (%)*	*min-max*
Age		49.59 ± 12.92	50.50 (40-58)	15-79
Gender; n (%)	Female	42 (55.26)		
	Male	34 (44.74)		
Sokal risk group; n (%)	Low	13 (21.31)		
	Intermediate	36 (59.02)		
	High	12 (19.67)		
EUTOS risk group; n (%)	Low	50 (87.72)		
	High	7 (12.28)		
Comorbidity; n (%)	Absent	32 (42.11)		
	Present	44 (57.89)		
	DM	10 (13.10)		
	HT	8(10.50)		
	CAD	8(10.50)		
	CHF	4(5.26)		
	Mechanic Valve	4(5.26)		
	Renal Disease	9(11.80)		
	Hypothyroidism	5(6.57)		
	Astma	2(2.60)		
	Malignant Disease	5(6.57)		
MMR at 6th Month; n (%)	MMR+	29 (38.20)		
	MMR-	28 (36.80)		
	Not Known	18 (25)		
MMR at 12th Month; n (%)	MMR+	48 (81.4)		
	MMR-	11 (18.6)		
Adherence to Treatment; n (%)	No	7 (9.2)		
	Yes	69 (90.8)		
Imatinib related side effect; n (%)	Absent	53 (69.74)		
	Present	23 (30.26)		
Switching to 2nd Generation TKIs n (%)	No	41 (53.95)		
	Yes	35 (46.05)		

Tablo 1. (Continued)

Reason for Switching; n (%)	Cytogenetic response failure	23 (65.70)		
	Loss of MMR	5 (14.30)		
	Side effect	7 (20)		
Outcome; n (%)	Alive	72 (94.74)		
	Death	4 (5.26)		
EFS		80.45 ± 71.65	67.98 (11.96 – 131.52)	1.35 – 237.37
OS		111.41 ± 62.87	99.56 (63.84 – 143.63)	13.57 – 274.37

EUTOS: European Treatment and Outcome Study, MMR: Major Molecular Response, TKIs: Tyrosine Kinase Inhibitors, EFS: Event Free Survival, OS: Overall Survival

When examining the response to imatinib therapy, it was observed that among 57 patients with known 6th-month IS data, 29 (38.2%) achieved MMR, while among 59 patients with 12th-month IS data, 48 (80%) achieved MMR. It was noted that treatment was changed in 22.3% (n=17) of patients before the 12th month due to non-responsiveness or side effects. Treatment adherence was observed in 90.8% (n=69) of patients, while 9.2% (n=7) were found to be non-adherent to therapy.

3.2. Molecular response and survival of the patients

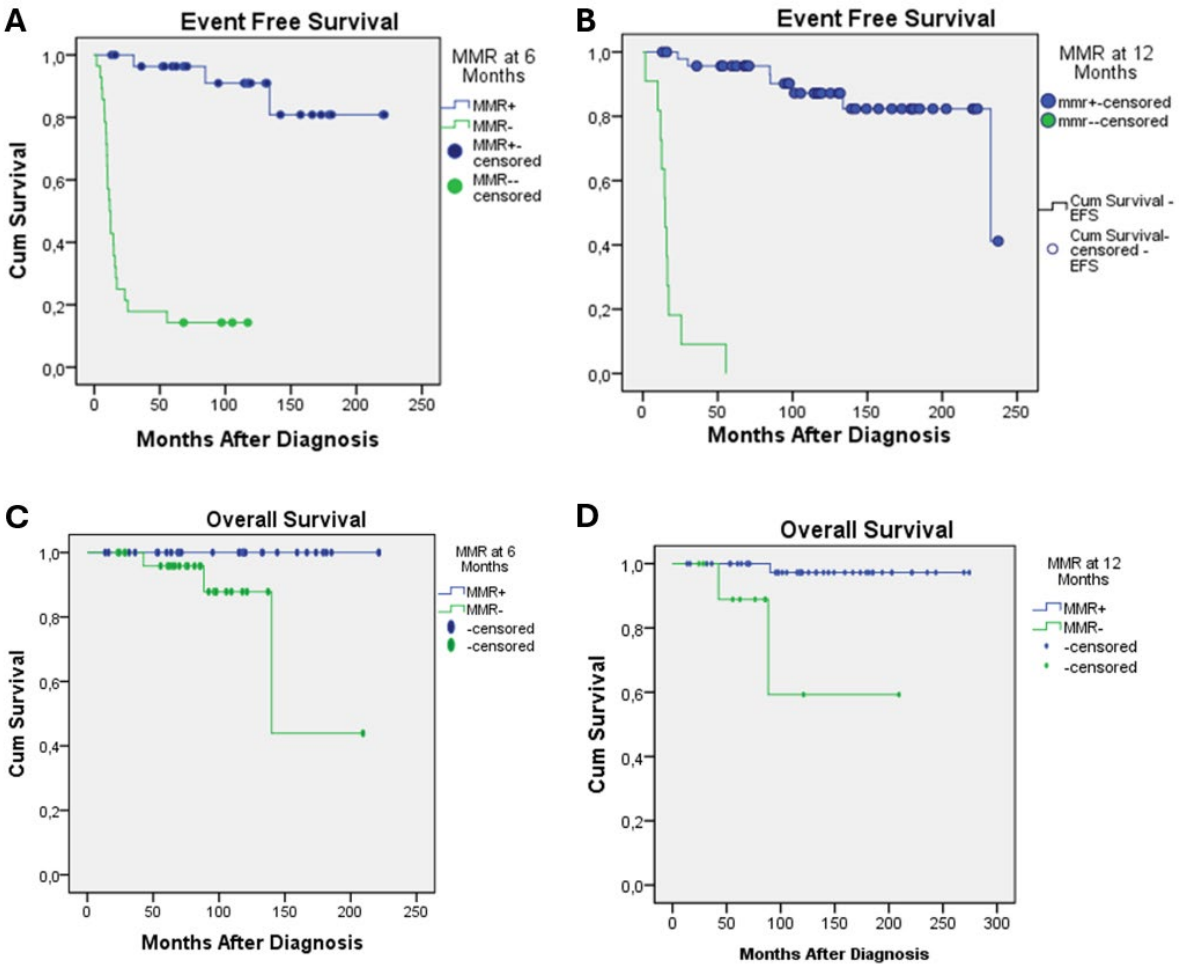
The median event-free survival (EFS) with imatinib was 80.45 ± 71.65 months (range: 1.35–237.37 months). The 10-year EFS rate was 54% (±0.059), while the 5-year EFS rate was 98.6% 60% (±0.057). During follow-up, it was noted that 35 patients (46.05%) switched to second-generation TKIs, and among these, 23 (65.7%) switched due to failure to achieve complete cytogenetic response, 5 (6.6%) due to loss of MMR, and 7 (9.2%) due to side effects. Factors affecting EFS revealed that patients who achieved MMR at the 6th and 12th months had significantly longer EFS (p<0.0001). (Figure 1) For patients who achieved MMR at the 6th month, the EFS was 198.09 ± 12.39 months (95% CI: 173.82–222.37), while it was 28.25 ± 7.09 months (95% CI: 14.36–42.14) for those who did not achieve MMR. For patients who achieved MMR at the 12th month, the EFS was 208.64 ± 10.0 months (95% CI: 189.04–228.23), while it was 17.79 ± 4.14 months (95% CI: 9.67–25.92) for those who did not. (Figure 1) It was found that the EUTOS and Sokal risk groups did not affect EFS (Table 2). Cox regression analysis showed that the failure to achieve MMR at the 6th month increased the risk of events by 28 times (p=0.0001), and the failure to achieve MMR at the 12th month increased the risk of events by 76 times (p=0.0001) (Figure 2)

As of the data cutoff date, it was observed that 53.9% (n=41) of the 76 patients were still maintaining major molecular response with imatinib therapy, 4 patients had died, and 31 (40.8%) patients were being followed with second-generation TKIs. Median OS was 111.41 ± 62.87 months (range: 13.57–274.37 months). 10-year overall survival was 94.2% (±0.033) and 5-year overall survival was 98.5% (±0.15) for the whole population. All four deceased patients had previously switched to 2ndGTKI therapy, and the causes of death were unrelated to CML (congestive heart failure, respiratory failure, subdural hematoma, chronic renal failure).

When examining factors affecting overall survival (OS), it was found that in patients aged ≥65 years, OS was 132.33 ± 18.27 months (95% CI: 96.51–168.14), while in patients under 65 years, OS was significantly longer at 266.31 ± 5.6 months (95% CI: 255.34–277.29) (p=0.002). It was observed that OS was shorter in patients who did not achieve MMR at the 6th (p=0.016) and 12th months (p=0.001). (Figure 1)

Figure 1. A.

Event-free survival according to MMR at 6th month. Patients with MMR at 6 months had significantly longer EFS than those without MMR (198.1 vs 28.3 months, respectively). ***B.*** *Event-free survival according to MMR at 12th month. Patients with MMR at 12 months had significantly longer EFS than those without MMR (208.6 vs 17.8 months, respectively).* ***C.*** *Overall survival according to MMR at 6th Month. OS was longer in patients with MMR at 6 months, and no deaths occurred among responders.* ***D.*** *Overall survival according to MMR at 12th month. Patients with MMR at 12 months had longer OS (269.3 vs. 155.0 months; p=0.001).*



MMR: Major Molecular Response, EFS: Event-free survival, OS: Overall survival

In patients who achieved MMR at the 12th month, OS was 269.25 ± 5.04 months (95% CI: 259.37–279.13), while it was 155.00 ± 32.10 months (95% CI: 92.08–217.93) for those who did not achieve MMR. None of the patients who achieved MMR at the 6th month died (Table 2).

Table 2.

Comparison of OS and EFS between groups

OS		n	Event n (%)	Mean ± S.E.	%95 C.I. Lower - Upper	Log-rank p
Overall (months)		76	4 (5.30)	256.95 ± 8.54	240.21 – 273.70	
MMR at 6th Month	MMR+	29	0 (0)	-	-	**0.016***
	MMR-	28	3 (10.70)	-	-	
MMR at 12th Month	MMR+	48	1 (2.10)	269.25 ± 5.04	259.37 – 279.13	**0.001***
	MMR-	11	2 (18.20)	155.00 ± 32.10	92.08 – 217.93	
Comorbidity	Absent	32	0 (0)			0.101
	Present	44	4 (9.10)			
Adherence to treatment	No	7	1 (14.30)	179.13 ± 26.17	127.84 – 230.42	0.234
	Yes	69	3 (4.30)	259.46 ± 8.56	242.68 – 276.25	
Imatinib Related Side Effect	No	53	2 (3.80)	261.31 ± 9.20	243.28 – 279.34	0.323
	Yes	23	2 (8.70)	186.61 ± 10.61	165.82 – 207.4	
Age	<65	68	2 (2.90)	266.31 ± 5.60	255.34 – 277.29	**0.002***
	≥65	8	2 (25)	132.33 ± 18.27	96.51 – 168.14	
Sokal Score	Low	13	0 (0)			0.347
	Intermediate	36	3 (8.30)			
	High	12	0 (0)			
EUTOS risk group	Low	50	3 (6)			0.448
	High	7	0 (0)			
Imatinib Failure	No	41	0 (0)			**0.006***
	Yes	35	4 (11.40)			
EFS		**n**	**Event n (%)**	**Mean ± S.E.**	**%95 C.I. Lower - Upper**	**Log-rank p**
Overall (months)		76	35 (46.10)	135.35 ± 12.67	110.51 – 160.19	
MMR at 6th Month	MMR+	29	3 (10.30)	198.09 ± 12.39	173.82 – 222.37	**0.0001***
	MMR-	28	24 (85.70)	28.25 ± 7.09	14.36 – 42.14	
MMR at 12th Month	MMR+	48	7 (14.60)	208.64 ± 10.0	189.04 – 228.23	**0.0001***
	MMR-	11	11 (100)	17.79 ± 4.14	9.67 – 25.92	
Comorbidity	Absent	32	15 (46.90)	126.28 ± 18.20	90.62 – 161.94	0.999
	Present	44	20 (45.50)	136.82 ± 16.90	103.70 – 169.94	

Tablo 2. (Continued)

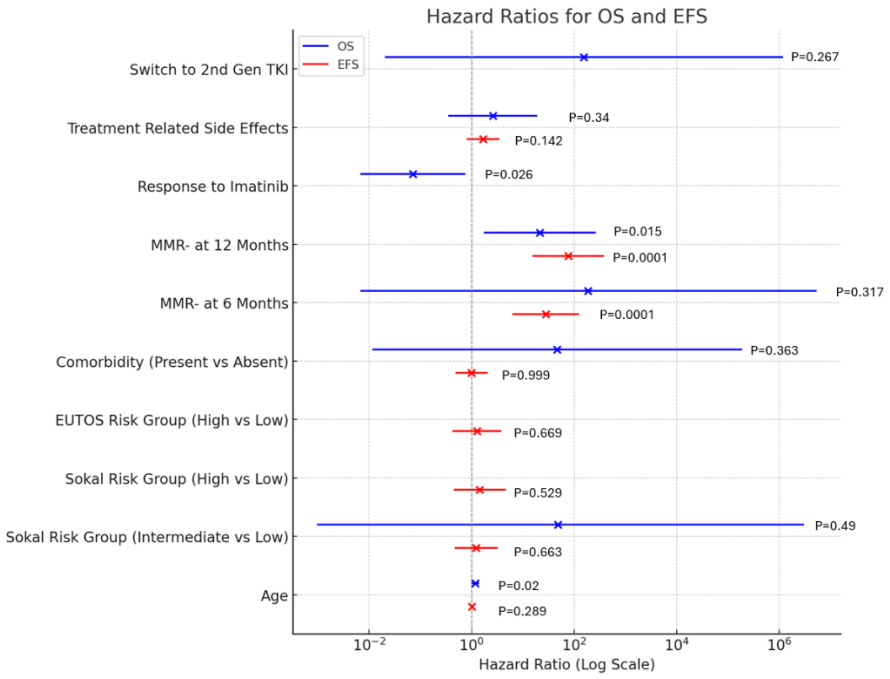
Adherence to Treatment	No	7	4 (57.10)	84.44 ± 27.34	30.86 – 138.03	0.589
	Yes	69	31 (44.90)	138.01 ± 13.28	111.98 – 164.04	
Imatinib related side effect	No	53	22 (41.50)	146.60 ± 14.97	117.26 – 175.95	0.138
	Yes	23	13 (56.50)	96.68 ± 19.16	59.12 – 134.24	
Age	<65	68	30 (44.10)	140.68 ± 13.26	114.69 – 166.67	0.094
	≥65	8	5 (62.50)	65.45 ± 25.70	15.07 – 115.83	
Sokal score	Low	13	6 (46.20)	131.23 ± 27.16	78 – 184.46	0.817
	Intermediate	36	17 (47.20)	120.39 ± 17.73	85.64 – 155.14	
	High	12	6 (50)	61.87 ± 15.93	30.66 – 93.09	
EUTOS risk group	Low	50	25 (50)	96.15 ± 11.99	72.66 – 119.64	0.664
	High	7	4 (57.10)	56.44 ± 20.01	17.22 – 95.67	

EUTOS: European Treatment and Outcome Study, MMR: Major Molecular Response, TKIs: Tyrosine Kinase Inhibitors, EFS: Event Free Survival, OS: Overall Survival

Cox regression analysis revealed that as the age at diagnosis increased, the risk of death also increased (HR: 1.17, p=0.02). The failure to achieve MMR at the 12th month (HR: 21.47, p=0.015) increased the risk of death, while achieving a response to imatinib therapy reduced the risk of death (HR: 0.072, p=0.026) (Figure 2).

Figure 2.

Cox regression analysis for risk factors. Higher age (HR: 1.17), absence of 12-month MMR (HR: 21.47), and no response to imatinib (HR: 0.072) were significant predictors of mortality (p<0.05, Cox regression)

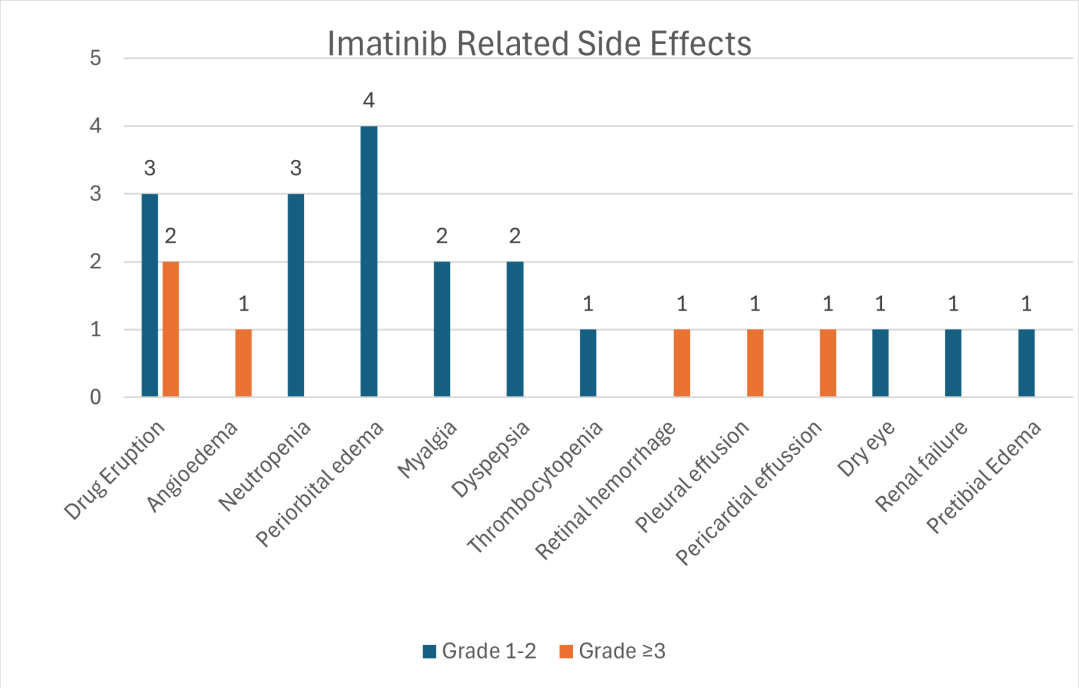


MMR: Major Molecular Response, EFS: Event-free survival, OS: Overall survival EUTOS: European Treatment and Outcome Study, 2nd Gen TKI: Second Generation Tyrosine Kinase Inhibitor

During the follow-up period, 23 patients (30.3%) experienced imatinib-related side effects. Seven patients (9.2%) experienced grade 3 side effects requiring treatment changes, while no grade 4–5 side effects were reported. Five of the grade 3 side effects occurred in the first year of treatment, one patient developed pericardial effusion in the seventh year, and one patient experienced a drug eruption in the eighth year. The side effects and their grades are shown in Figure 3.

Figure 3.

Imatinib related side effects. During follow-up, 30.3% of patients experienced imatinib-related side effects, while 9.2% developed grade 3 adverse events requiring treatment modification



4. DISCUSSION

Imatinib mesylate has transformed the treatment of chronic myeloid leukemia (CML), dramatically improving clinical outcomes and patient survival. As a tyrosine kinase inhibitor specifically targeting the BCR-ABL fusion protein, imatinib has become the standard first-line therapy for CML patients in chronic phase.[12] It has demonstrated remarkable efficacy, generating unprecedented rates of complete hematologic and cytogenetic responses, as well as sustained reductions in BCR-ABL transcripts. The results of our study showed that failure to achieve MMR by the 12th month and advanced age are risk factors for death. At the end of follow-up, 53.9% of patients remained on imatinib, all of whom were alive. Response to imatinib was significantly associated with reduced risk of death. Failure to achieve MMR at the 6th and 12th months increases the risk of disease progression and decreases the EFS. The 10-year OS and EFS rates were 94.2% and 54%, while the 5-year OS and EFS rates were 98.5% and 60%, respectively, for the entire population.

The long-term results of the IRIS study, published in 2017, indicate that the estimated 10-year survival rate with imatinib treatment is 83.3%, 10-year EFS is 79.6%. Approximately half (48.3%) of the patients in this study were able to continue imatinib treatment until the end of the study and 82.8% had a complete cytogenetic response.[5] A total of 861 patients with CP-CML were included in a recent study analyzing real-life data in Turkey. After 5.1 years of follow-up, 49.4% of patients continued on imatinib treatment, while 60% switched to second-generation TKI treatment due to non-response or loss of response to imatinib.[13] One-year, five-year, and ten-year OS rates were 99.2%, 93.7%, and 89.1%, respectively, showcasing favorable long-term outcomes in the era of tyrosine kinase inhibitors (TKIs). In our study possibly because of the insufficient number of patients included, OS is much longer than other

studies as 94.2% for 10 years. Similar to our findings, a Polish study reported an 10-year OS rate of 98.82% for 267 patients. However, they achieved a longer 10-year event-free survival (EFS) of 88.7%, which is better than our results.[14] The shorter EFS in our population is due to our switching policy to 2nd generation TKIs based on periodic IS measurement; cytogenetic response is deemed acceptable only for patients with multiple comorbidities and the period before the approval of 2nd generation TKIs.

In our study, we found that patient adherence to imatinib treatment was 90.8%. The ADAGIO (Adherence Assessment with Glivec: Indicators and Outcomes) study, a large-scale research effort conducted in Belgium, prospectively examined adherence to imatinib over a 90-day period with a sample of 169 patients. The findings revealed that one-third of the patients were considered nonadherent. Additionally, only 14.2% of the patients demonstrated perfect adherence, taking 100% of their prescribed imatinib.[15]

Our study's rate of achieving MMR at 12 months with imatinib was 80%. These results are higher than those of the IRIS study, in which 305 patients could be evaluated for 12-month MMR measurement, and MMR achievement was 50.2%. Other studies that compare the efficacy of imatinib vs 2nd-generation TKIs revealed that 12th month MMR achievement with imatinib is below 30%.[12,16–18] The reason for the higher MMR at 12 months in our study is probably the insufficient number of patients who underwent molecular analyses and the fact that we switched to second-generation TKIs in non-responders with BCR::ABL IS>10% at 6 months. Therefore, a high proportion of the remaining patients were already responsive to imatinib. We also believe that treatment adherence is an important factor in achieving MMR at 12 months.

When we look at the prognostic factors that affect survival, a study from Turkey reported that being female, absence of cardiovascular disease at diagnosis, presence of molecular response, and presence of cytogenetic response were independent predictors of longer survival.[13] A Rwandan population-based analysis found that age >45, white blood cell count, Rwandan residence, primary and secondary resistance to imatinib increased the risk of mortality.[19] When we looked at our results in concordance with other trials; older age, unresponsive to imatinib treatment and not achieving MMR at the 12th month increased the risk of death.

Approximately 31% of patients in the Turkish cohort had at least one comorbidity at diagnosis, with cardiovascular diseases (13.9%) and diabetes mellitus (10.5%) being the most common.[13] Patients with cardiovascular disease or diabetes had significantly shorter survival compared to those without these comorbidities. Following this trial, our patient group had similar comorbidities with 21% (n:12) of them having cardiac disease and 13.1% having diabetes mellitus. However, we didn't find any relationship between comorbidities and OS.

Imatinib is considered the safest among tyrosine kinase inhibitors (TKIs), with over two decades of clinical use. Its long-term safety profile is well established, with no known irreversible adverse effects, making it a reliable option for patients. According to the results of our study, 3 patients (3.9%) receiving imatinib had ≥grade 3 drug-related adverse events (pleural and pericardial effusion, retinal hemorrhage) during the follow-up period. The results of the IRIS study revealed that a total of 51 of 551 patients (9.3%) had a serious adverse event (most frequently abdominal pain). Serious adverse events most frequently occurred during the first year of treatment.[5] Randomized controlled trials that compare 2GTKIs and imatinib again demonstrate the safety of imatinib treatment. Thrombocytopenia, cardiovascular events, pancreatic and hepatic effects were more frequent among the patients treated with second- and third-generation TKIs.[20–23]

An important limitation of our study is that it was conducted as a single-center trial. Additionally, an insufficient number of patients underwent molecular analysis at the 3rd, 6th, and 12th months.

5. CONCLUSION

Imatinib has a two-decade history of demonstrated efficacy and safety, and it is now

widely available in generic form, leading to a significant reduction in cost. Results from this single-center study indicate that imatinib is effective and safe in treating patients with chronic myeloid leukemia (CML). Molecular monitoring plays a crucial role in identifying patients who do not respond to imatinib within the first three to six months, allowing for the introduction of more potent therapies. Notably, some high-risk patients can still respond well to imatinib, regardless of their prognostic scores, such as the Sokal or EUTOS scores. Furthermore, achieving a MMR by the twelfth month is an important predictor of both event-free survival and overall survival.

Article Information Form

Authors Notes

The part of the article was presented as a poster presentation at the 22th National Hematology Congress held on 1-5 November 2022.

Acknowledgments

Authors would like to express their gratitude to all those colleagues involved in reporting patients and collecting data.

Funding

Authors has no received any financial support for the research, authorship or publication of this study.

Authors' Contribution

All authors contributed to the study's conception and design. N.A.A. designed the study, controlled the data, managed the care of the patients, interpreted the results, and drafted the article, Ö.E, K.K, İ.C.K managed the patients' care, made the data entry, controlled the data of the patients, interpreted the results, Hande Senol controlled the data, interpreted the results and performed the statistical analysis and Nil Güler was involved in the design of the study and interpretation of the results. All authors reviewed the last version of the manuscript and made interpretations.

The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by authors.

Artificial Intelligence Statement

No artificial intelligence tools were used while writing this article.

Copyright Statement

REFERENCES

1. Faderl S, Talpaz M, Estrov Z, O'Brien S, Kurzrock R, Kantarjian HM. The biology of chronic myeloid leukemia. *N Engl J Med.* 1999;341:164–172.
2. Sokal JE, Cox EB, Baccarani M, Tura S, Gomez GA, Robertson JE *et al.* Prognostic Discrimination in "Good-Risk" Chronic Granulocytic Leukemia. *Blood.* 1984;63:789–799.
3. Hasford J, Baccarani M, Hoffmann V, Guilhot J, Saussele S, Rosti G et al. Predicting complete cytogenetic response and subsequent progression-free survival in 2060 patients with CML on imatinib treatment: The EUTOS score. *Blood.* 2011;118:686–692.
4. Bower H, Björkholm M, Dickman PW, Höglund M, Lambert PC, Andersson TM-L. Life expectancy of patients with chronic myeloid leukemia approaches the life expectancy of the general population. *J Clin Oncol Off J Am Soc Clin Oncol.* 2016;34:2851–2857.
5. Hochhaus A, Larson RA, Guilhot F, Radich JP, Branford S, Hughes TP et al. Long-term outcomes of imatinib treatment for chronic myeloid leukemia. *N Engl J Med.* 2017;376:917–927.
6. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood.* 2016;127:2391–2405.
7. Hughes T, Deininger M, Hochhaus A, Branford S, Radich J, Kaeda J et al. Monitoring CML patients responding to treatment with tyrosine kinase inhibitors: Review and recommendations for harmonizing current methodology for detecting BCR-ABL transcripts and kinase domain mutations and for expressing results. *Blood.* 2006;108:28–37.

8. Alaggio R, Amador C, Anagnostopoulos I, Attygalle AD, Araujo IB de O, Berti E et al. The 5th edition of the World Health Organization classification of haematolymphoid tumours: Lymphoid neoplasms. *Leukemia.* 2022;36:1720–1748.
9. Hochhaus A, Baccarani M, Silver RT, Schiffer C, Apperley JF, Cervantes F et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leukemia.* 2020;34:966–984.
10. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. U.S. Department of Health and Human Services. Published November 27, 2017. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/ctcae_v5_quick_reference_5x7.pdf
11. Cross NCP, White HE, Colomer D, Ehrencrona H, Foroni L, Gottardi E et al. Laboratory recommendations for scoring deep molecular responses following treatment for chronic myeloid leukemia. *Leukemia.* 2015;29:999–1003.
12. Claudiani S, Apperley JF. The argument for using imatinib in CML. *Hematol (United States).* 2018;2018:161–167.
13. Saydam G, Unal A, Haznedaroglu IC, Hacihanifioglu A, Mehtap O, Kurtoglu E et al. Turkey Real-Life Data: Demographic Features, Treatment Results and Effects of Comorbidities in Chronic Myeloid Leukemia. *Int J Hematol Oncol.* 2022;11:IJH40.
14. Szczepanek E, Chukwu O, Kamińska M, Wysogląd H, Cenda A, Zawada M et al. Long-term outcomes of patients with Chronic Myeloid Leukemia who commenced treatment with imatinib: A 20-year single-centre experience. *Leuk Lymphoma.* 2022;63:2213–2223.
15. Noens L, van Lierde M-A, De Bock R, Verhoef G, Zachée P, Berneman Z et al. Prevalence, determinants, and outcomes of nonadherence to imatinib therapy in patients with chronic myeloid leukemia: The ADAGIO study. *Blood.* 2009;113:5401–5411.
16. Signorovitch J, Ayyagari R, Reichmann WM, Wu EQ, Chen L. Major molecular response during the first year of dasatinib, imatinib or nilotinib treatment for newly diagnosed chronic myeloid leukemia: A network meta-analysis. *Cancer Treat Rev.* 2014;40:285–292.
17. Jabbour E, Kantarjian HM, Saglio G, Steegmann JL, Shah NP, Boqué C et al. Early response with dasatinib or imatinib in chronic myeloid leukemia: 3-year follow-up from a randomized phase 3 trial (DASISION). *Blood.* 2014;123:494–500.
18. Kantarjian HM, Hochhaus A, Saglio G, De Souza C, Flinn IW, Stenke L et al. Nilotinib versus imatinib for the treatment of patients with newly diagnosed chronic phase, Philadelphia chromosome-positive, chronic myeloid leukaemia: 24-month minimum follow-up of the phase 3 randomised ENESTnd trial. *Lancet Oncol.* 2011;12:841–851.
19. Morgan J, DeBoer RJ, Bigirimana JB, Nguyen C, Ruhangaza D, Paciorek A et al. A ten-year experience of treating chronic myeloid leukemia in rural Rwanda: Outcomes and insights for a changing landscape. *JCO Glob Oncol.* 2022;8:1–10.
20. Lipton JH, Chuah C, Guerci-Bresler A, Rosti G, Simpson D, Assouline S et al. Ponatinib versus imatinib for newly diagnosed chronic myeloid leukaemia: An international, randomised, open-label, phase 3 trial. *Lancet Oncol.* 2016;17:612–621.
21. Gambacorti-Passerini C, Cortes JE, Lipton JH, Dmoszynska A, Wong RS, Rossiev V et al. Safety of bosutinib versus imatinib in the phase 3 BELA trial in newly diagnosed chronic phase chronic myeloid leukemia. *Am J Hematol.* 2014;89:947–953.
22. Hochhaus A, Saglio G, Hughes TP, Larson RA, Kim D-W, Issaragrisil S et al. Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloid leukemia in chronic phase: 5-year update of the randomized ENESTnd trial. *Leukemia.* 2016;30:1044–1054.
23. Cortes JE, Saglio G, Kantarjian HM, Baccarani M, Mayer J, Boqué C et al. Final 5-Year Study Results of DASISION: The Dasatinib Versus Imatinib Study in Treatment-Naïve Chronic Myeloid Leukemia Patients Trial. *J Clin Oncol Off J Am Soc Clin Oncol.* 2016;34:2333–2340.