Early Predictors of Treatment-free Remission in Chronic Myeloid Leukemia

Aziz Farhat[1], Georgina El Hajjar[1], Hagop Kantarjian[1], Fadi G. Haddad[1], Nicholas J. Short[1], Guillermo Montalban-Bravo[1], Danielle Hammond[1], Elias Jabbour[1], Guillermo Garcia-Manero[1], Koji Sasaki[1], Ghayas C. Issa[1]

[1]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Abstract

Background: Tyrosine kinase inhibitors (TKIs) have markedly improved outcomes in chronic myeloid leukemia (CML), making treatment-free remission (TFR) a key goal, especially for younger patients. While current TFR criteria require sustained deep molecular remission after years of therapy, early predictors are lacking. This study aimed to identify factors associated with TFR eligibility.

Methods: We reviewed 780 patients with newly diagnosed chronic phase CML treated at MD Anderson from 2012–2023. Of these, 412 (53%) met NCCN criteria for TFR (sustained MR4.5 for 2 years after 3 years of therapy). After excluding 30 patients with insufficient treatment duration, 338 (43%) formed the control group. We compared both cohorts and analyzed predictors of TFR eligibility using logistic regression.

Results: TFR-eligible patients were older (median age 51 vs. 46; P = 0.007), had more favorable Sokal risk profiles (P = 0.037), and different TKI usage (P = 0.01), with more receiving dasatinib. The e14a2 BCR::ABL transcript was more frequent in the TFR group (46% vs. 32%; P < 0.001), while resistance mutations were exclusive to the control group (13%). Univariate analysis identified older age, BCR::ABL halving-time <30 days, early molecular responses, e14a2 transcript, co-expression of e13a2/e14a2, and use of newer TKIs as predictive. Multivariate analysis confirmed older age (OR: 1.02; P = 0.045), halving-time <30 days (OR: 2; P = 0.041), MMR at 1 year (OR: 5.6; P < 0.001), and e14a2 transcript (OR: 1.6; P = 0.049) as independent predictors.

Conclusion: Older age, rapid BCR::ABL decline, early molecular milestones, and e14a2 transcript independently predict TFR eligibility. These markers may serve as early TFR surrogates in future trials.

Introduction

• **TKIs have dramatically improved outcomes for CML**, allowing most patients to achieve near-normal life expectancy.

• **The focus of therapy has shifted toward achieving treatment-free remission (TFR)**, particularly in younger patients, but early predictors of TFR eligibility are currently lacking.

Aim

• We sought to delineate the early predictors of treatment-free remission.

Methods

• Reviewed 780 CML patients treated at MD Anderson (2012–2023).

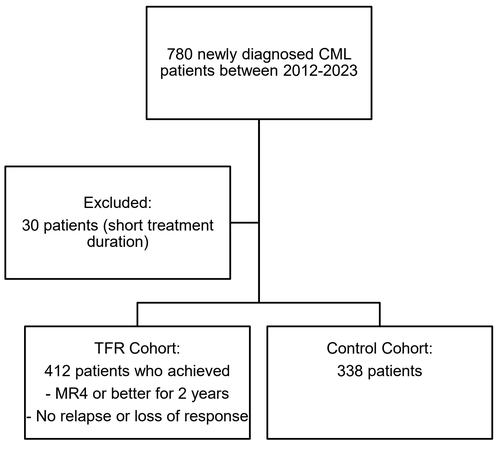
• Identified 412 TFR-eligible patients; excluded 30 for short treatment; 338 formed the control group.

• Compared clinical and molecular features between groups

• Performed **univariate logistic regression** to screen potential predictors of TFR eligibility.

• Included variables with **P < 0.1** in a **multivariate logistic regression** to identify independent predictors.

Patient Selection



Results

Baseline characteristics between both groups

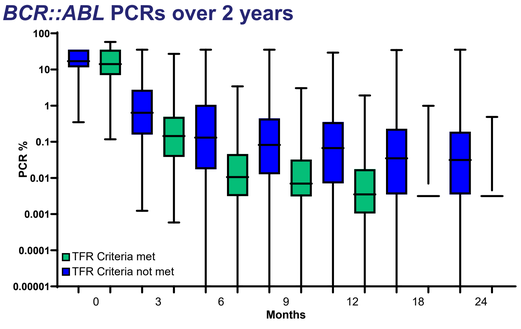
Covariate	TFR Cohort (n=412)	Control Cohort (n=338)	*P*
Age, median [range]	51 [19-85]	46 [15-86]	0.007
Female, n (%)	179 (43)	150 (44)	0.8
Sokal score category			0.037
Low, n (%)	276 (67)	217 (64)	
Intermediate, n (%)	112 (27)	84 (25)	
High, n (%)	24 (6)	37 (11)	
Tyrosine kinase inhibitor			0.01
Imatinib, n (%)	130 (32)	138 (41)	
Dasatinib, n (%)	178 (43)	110 (33)	
Nilotinib, n (%)	80 (19)	63 (19)	
Ponatinib, n (%)	24 (6)	27 (8)	
***BCR::ABL* transcript**			<0.001
e13a2, n (%)	137 (33)	171 (51)	
e14a2, n (%)	190 (46)	107 (32)	
e13a2+e14a2, n (%)	85 (21)	54 (16)	
Other variants, n (%)	0 (0)	6 (1)	
***ABL* mutations, n (%)**	0 (0)	44 (13)	-

Outcomes for pts across both groups:

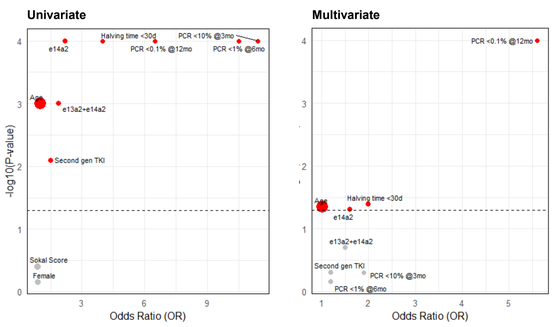
Response	TFR Cohort (n=412)	Control Cohort (n=338)	*P*
Halving time at 3 months, median [range]	13.7 [6.5-602.4]	17.2 [3.6-485.9]	<0.001
Fold decrease at 3 months, median [range]	108 [0.4-11222]	34 [0.1-11222]	<0.001
ELN milestones			
PCR <10% IS (EMR) at 3 months (M3)	361/365 (99)	222/250 (89)	<0.001
PCR <1% IS (MR) at 6 months (M6)	373/399 (93)	189/249 (76)	<0.001
PCR <0.1% IS (MMR) at 12 months (M12)	366/392 (93)	138/241 (57)	<0.001

Responses were reported as no. achieved/no. evaluable, (%)

BCR::ABL PCRs over 2 years



Log Regression Analysis:



Conclusion

• **Older age**, **BCR::ABL halving-time <30 days**, and **MMR at 1 year** are independent predictors of TFR eligibility.

• The **e14a2 BCR::ABL transcript** is associated with higher likelihood of achieving TFR.

• These factors may serve as **early surrogates** to guide future **TFR-focused clinical trials**.

Correspondence:
Ghayas C. Issa, MD.
The University of Texas MD Anderson Cancer Center,
Department of Leukemia, 1515 Holcombe Boulevard,
Houston, TX 77030, USA.
Email: GCIssa@mdanderson.org