Abstract: P716

Title: IMPROVEMENT OF TREATMENT-FREE REMISSION RATE FOLLOWING DISCONTINUATION OF BCR::ABL1 TKI WITH A FASTER INITIAL DECLINE OF BCR::ABL1 TRANSCRIPT AND LONGER TREATMENT DURATION IN CHRONIC MYELOID LEUKEMIA

Abstract Type: Poster Presentation

Topic: Chronic myeloid leukemia - Clinical

Background:

Over recent years, numerous clinical studies have demonstrated that approximately one-half of patients with chronic phase chronic myeloid leukemia (CP-CML) who receive sufficient tyrosine kinase inhibitors (TKIs) and achieve and maintain a deep molecular response (DMR) are able to successfully discontinue therapy. In this context, Treatment free remission (TFR) is a major goal for all CML patients according to the current guidelines and the main factors affecting TFR are the duration of TKIs treatment and the duration of DMR maintenance during TKI treatment.

Aims:

This study analyzed the TFR success rate in CP-CML patients who maintained DMR for 4 years or more and investigated whether new clinical application criteria could be derived with TFR study of longer TKI treatment duration and DMR duration.

Methods:

Among patients newly diagnosed with CP-CML and treated at least one of TKIs (Imatinib, Nilotinib, Dasatinib, Bosutinib, and Radotinib) as the first treatment, patients who maintained MR4.5 (*BCR::ABL1* IS ≤0.0032%) continuously for at least 4 years through reverse transcriptase quantitative polymerase chain reaction (RT-qPCR) tests were enrolled in this study. After discontinuation, molecular responses were monitored using the RT-qPCR method. In the case of relapse, defined as loss of major molecular response (MMR), the last TKI therapy with same dose was reintroduced, and molecular responses after resumption were monitored monthly until achievement of MMR using RT-qPCR.

Results:

Altogether 116 patients (50 males and 66 females) discontinued TKI. Median age at diagnosis was 43.0 years (range, 40.8-45.3) and the percentages of patients with low, intermediate and high Sokal risk scores ware 58 (50.0%), 35 (30.2%) and 18 (15.5%) patients, respectively with unknown Sokal risk scores in 5 (4.3%) patients. The percentage of patients with low and high EUTOS scores was 69.8% and 6.0%, respectively and 24.1% had an unknown risk. Prior to discontinuation, all patients received TKIs for a median of 118.0 months (range, 63.6-224.7), and the duration of sustained MR4.5 was 67.4 months (range, 48.6-157.9). At the time of discontinuation, 93 patients (80.2%) were using first-line TKI. The patient-specific calculated halving time of BCR::ABL1 after starting TKI treatment to determine early molecular kinetics was median 11.1 days (range, 3.3-722.2).

After a median follow-up from treatment discontinuation of 28.0 months (range, 10.9-150.7), the TFR rates at 12, 24, and 48 months were 81.9%, 76.0%, and 71.0%, respectively (Figure 1). 88 patients were still free of treatment with sustained MR4.5. Despite 45 patients losing UMRD, 17 patients were able to regain their MMR, while 28 (24.1%) patients have lost MMR at a median of 8.4 months (range, 1.8-42.0) after discontinuation; 18 (64.3%) patients had molecular relapse within 6 months of TKI discontinuation. No progression toward advanced-phase CML occurred, and when 28 patients who lost MMR were retreated with same TKI, 26 patients (92.9%) re-achieved MMR with a median of 5.6 months (range, 2.3-23.4). Variables demonstrating a significant association on univariate analysis were EUTOS risk score, total duration of TKI therapy and halving time.

Summary/Conclusion:

Our result demonstrates that TFR rate can be improved in patients who received TKI treatment for approximately 10 years and maintained DMR for more than 6 years regardless of the type of TKI. Based on results, we can confirm that a more rapid initial *BCR::ABL1* decline after commencing TKI and total duration of TKI therapy correlated with an increased probability of achieving TFR eligibility.

Characteristic	All Patients (N=116)
Age, median (range)	43.0 (40.8-45.3)
Sex, N (%)	
Male	50 (43.1)
Female	66 (56.9)
Sokal score, N (%)	
Low	58 (50.0)
Intermediate	35 (30.2)
High	18 (15.5)
N/A	5 (4.3)
EUTOS, N (%)	
Low	81 (69.8)
High	7 (6.0)
N/A	28 (24.1)
Halving time	
Value available, N (%)	64 (55.2%)
Median halving time, day	11.1 (3.3-722.2)
Duration of TKI treatment, month	
Time from TKI start to cessation, median (range)	118.0 (63.6-224.7)
Time from 1st. MR4.0 to TKI cessation, median (range)	77.8 (48.6-157.9)
Time from 1st. MR4.5 to TKI cessation, median (range)	67.4 (48.6-157.9)
Follow-up duration (months), median (range)	28.0 (10.9-150.7)
Loss of UMRD, N (%)	45 (38.8)
Loss of MMR, N (%)	28 (24.1)
CMR re-achievement, N (%)	26 (92.9%, 26/28)
Time to CMR re-achievement, months (range)	5.6 (2.3-23.4)

Univariable Analysis	HR	95% CI	*P*
EUTOS risk score Low High	5.184	1.913-14.044	.001
Halving time, days <11.1 ≥11.1	4.183	1.149-15.225	.030
TKI duration, months <118.0 ≥118.0	0.384	0.169-0.873	.022

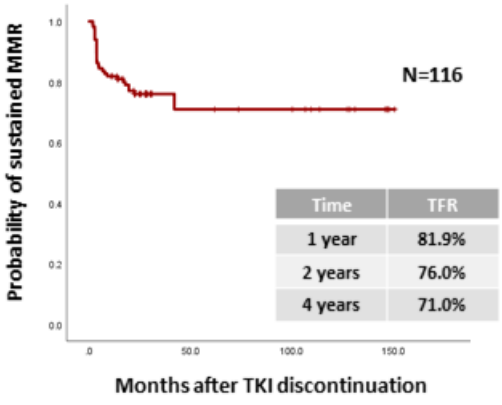

Figure 1. Treatment-free remission rates overall

Keywords: treatment-free remission, Chronic myeloid leukemia, Tyrosine kinase inhibitor, BCR::ABL