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POSTER ABSTRACTS

632.CHRONIC MYELOID LEUKEMIA: CLINICAL AND EPIDEMIOLOGICAL

Prospective Assessment of Co-Morbidities and Framingham Risk Score in Newly Diagnosed Chronic Myeloid Leukemia (CML) Patients and Its Impact on Clinical Outcomes Following Frontline TKI Therapy: Toronto CML Genomic Alliance in Greater Toronto Area & Ontario (TCGA-GTA)

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Introduction

Front-line (1L) tyrosine kinase inhibitor (TKI) drug selection is a pearl of clinical practice in CML. It requires consideration of multiple aspects including the goal of therapy, potency of the drug as well as comorbidity of the patient (pt). Contemporary CML practice emphasizes the importance of comorbidity for TKI selection. However, such data is scarce particularly the prevalence of comorbidity and its impact on 1L drug selection.

We are developing a shared care model with community hematologists in Greater Toronto Area (TCGA-GTA). Newly diagnosed CML pts in the community will be referred to the study core center for prospective enrolment into the CML registry, informed consenting for genetic testing/future research, and evaluation of baseline comorbidity. Pt will return to referring hematologists for management of CML, including 1L TKI treatment as per standard of care, and is scheduled to visit the study center at 6 and 12 months, then annually for 10 years. It gives us a unique opportunity to evaluate the impact of comorbidity on 1L TKI drug selection.

Patients and method

Adult pts with newly diagnosed CML of any phase within 2 months of diagnosis are eligible for the study unless they are not able to visit study core center. Comorbidities and Framingham risk score (FRS) were assessed at the time of initial evaluation. Mutation profile testing is done by a bar-coded error-corrected sequencing platform for 40 genes developed at the Ontario Institute for Cancer Research. Cumulative incidence of molecular response with 2 log (MR2), 3 log (MR3), 4 log reduction or deeper (MR4), and treatment failure (TF) were calculated using cumulative incidence method considering competing risk. Event-free survival (EFS) was defined as time from start of TKI until TKI stop/switch, TF or death. Failure-free survival (FFS) was defined as time from start of TKI to TF [primary resistance, loss of complete cytogenetic response, new additional cytogenetic abnormalities (ACAs), and progression to accelerated or blasts phase (AP/BP)] or death.

Results

From November 2020 until June 31, 2023 (data cutoff), a total of 77 pts were enrolled in the study. The median follow-up time was 12 months. The frequency of 1L TKI selection was as follows: IMATINIB (IM) (n=23, 30%), DASATINIB (n=25, 32%), NILOTINIB (n=22, 29%), BOSUTINIB (n=1, 1%), ASCIMINIB (n=6, 8%). Majority of the pts were male (n=51, 66%). Ninety-three percent of pts were in chronic phase at diagnosis, while 4% and 3% were in AP and BP, respectively. Presence of ACAs was detected in 18 pts (23%), 10 of which were high risk, while 6% (n=5) were not evaluable.

The baseline clinical and disease characteristics of pts on 1L IM vs other TKIs (2G-TKI) are summarised in **Table 1**. Of note, pts on IM were significantly older with higher FRS and comorbidities, including coronary artery disease, diabetes mellitus, and hypertension. The OS of all pts at 1 year was 98.5% (95% confidence interval 90%-99.8%). At 1 year, pts with intermediate to high risk FRS had lower FFS (73.2% vs 86.5%, p=0.037) while history of hyperlipidemia was associated with lower EFS (59.3% vs 81.5%, p=0.023) and 6 times more likely to stop or switch therapy due to intolerance or resistance (HR 5.9, p=0.002). Baseline comorbidities did not demonstrate signifincant impact on MR2 and MR3 at 1 year but pts with low FRS were more likely to achieve MR4 within 1 year (22.3% vs 0%, p=0.023). Age did not affect any of the clinical and molecular endpoints. Compared to 2G-TKI, IM had worse EFS (HR 3.93, p=0.003), FFS (HR 5.66, p=0.011), and MR2 (47.3% vs 84.4%, p=0.003) at 1 year. Further, IM pts experienced higher rate of any side effects compared to those on 2G-TKI (69.6% vs 31.5%, p=0.003).

Conclusion

The TCGA-GTA study provides valuable insights into the impact of comorbidity on selection of 1L TKI and its outcome in a real-world setting. Pts who are older and with higher FRS and comorbidities tend to receive 1L IM. However, pts on 1L 2G TKIs are more likely to reach treatment goals faster with lower probability of TF. The present study did not reach a clear conclusion whether the worse outcomes in the pts receiving IM are from IM treatment or concurrent risk factors such as age and comorbidities, thus further study with an expanded cohort and longer follow-up is required. Elderly pts or those with comorbidities would need alternative treatment with better efficacy and tolerability, such as Asciminib, that can overcome comorbidity issues in the future.

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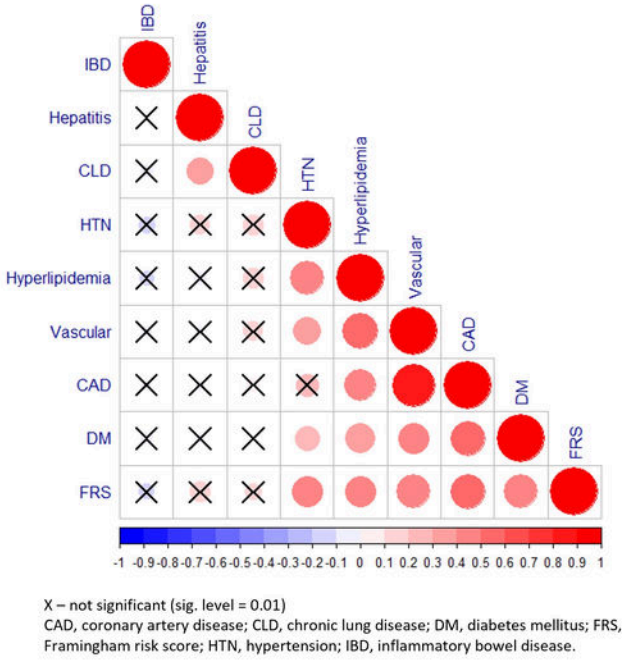
Table 1. Baseline clinical characteristics

	Imatinib (n=23)	2G-TKI (n=54)	p.value
Age, median (range)	**67 (22-84)**	**41 (34-77)**	**<0.001**
≥65y, n (%)	**12 (52.2)**	**5 (9.3)**	**<0.001**
Male, n (%)	14 (60.9)	37 (68.5)	0.601
Sokal Category, n (%)			
▪ Low	3 (13.0)	14 (25.9)	0.127
▪ Intermediate	15 (65.2)	21 (38.9)	
▪ High	5 (21.7)	19 (35.2)	
FRS, n (%)			
▪ **Low risk**	**7 (30.4)**	**49 (90.7)**	**<0.001**
▪ **Intermediate**	**7 (30.4)**	**3 (5.6)**	
▪ **High**	**9 (39.1)**	**2 (3.7)**	
mean (SD)	**18.10 (13.18)**	**4.45 (6.04)**	**<0.001**
Any comorbidities, n (%)	**16 (69.6)**	**18 (33.3)**	**0.005**
Coronary artery disease, n (%)	**5 (21.7)**	**0 (0.0)**	**0.002**
Chronic lung disease, n (%)	3 (13.0)	6 (11.1)	1
Diabetes mellitus, n (%)	**7 (30.4)**	**0 (0.0)**	**<0.001**
Hepatitis, n (%)	1 (4.3)	0 (0.0)	0.299
Hyperlipidemia, n (%)	7 (30.4)	9 (16.7)	0.222
Hypertension, n (%)	**11 (47.8)**	**11 (20.4)**	**0.026**
Inflammatory bowel disease, n (%)	2 (8.7)	0 (0.0)	0.086
Vascular disease[a], n (%)	4 (17.4)	2 (3.7)	0.062

FRS, Framingham risk score
[a]stroke, peripheral vascular disease, coronary disease

Figure 1. Correlation between FRS and comorbidities.



X – not significant (sig. level = 0.01)
CAD, coronary artery disease; CLD, chronic lung disease; DM, diabetes mellitus; FRS, Framingham risk score; HTN, hypertension; IBD, inflammatory bowel disease.

Figure 1

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