CO-EXISTING MYELOID MUTATIONS AT DIAGNOSIS ARE ASSOCIATED WITH INCREASED TYROSINE KINASE INHIBITOR UTILIZATION IN CHRONIC PHASE CML

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BACKGROUND

Co-existing myeloid mutations are increasingly being identified in chronic-phase CML. Although *ASXL1* has been associated with inferior outcomes, the broader effect of these mutations on treatment course, TKI utilization, and therapeutic durability remains incompletely characterized.

OBJECTIVES

To determine whether co-existing myeloid mutations are associated with differences in baseline characteristics, molecular response, TKI utilization, and treatment durability in patients with CML-CP.

METHODS

We retrospectively analyzed patients with CML-CP and stratified them by the presence of co-existing myeloid mutations into mutation-positive (M+) or mutation-negative (M-) cohorts.

Baseline characteristics, molecular responses, TKI utilization, and reasons for discontinuation were compared between cohorts.

CONCLUSION

Patients with co-existing myeloid mutations appeared to experience a more complex therapeutic course characterized by increased TKI switching and need for later-generation TKIs.

CONTACT INFORMATION

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RESULTS

Table 1: Patient Characteristics and Outcomes by Myeloid Mutation Status*

	M -	M +	p
Number, n (%)	133 (84.71%)	24 (15.28%)	
Age, median (range)	52.42 (13-89.99)	47.98 (22.44-71.09)	**0.07**
Male Sex, n(%)	**60 (45.1%)**	**16 (66.7%)**	**0.05**
WBC, median (IQR)	64.50 (30.38-177.8)	76.40 (41.44-189)	0.52
HgB, median (IQR)	11.85 (11.03-13.78)	12(10.77-13.08)	0.78
PLT, median (IQR)	381(240.5-533.5)	327(193-563)	0.44
PB Blast %, median (IQR)	1(0-3.5)	1(0.550-2.875)	0.67
IS %, median (IQR)	66.87(44.54-94.71)	49.38(36-61.71)	0.22
Standard Cytogenetics, n (%)	68(81.9%)	11(91.7%)	0.40
MMR or deeper response, n (%)	112 (84.2%)	19 (79.2%)	0.72
Time to best response in yrs, median (IQR)	4.05(1.95-2.27)	4.10(2.47-10.45)	0.22
Follow up in yrs, median (range)	8.73(0.14-25.79)	6.94 (0.81-29.57)	0.78

*** M-**, no coexisting myeloid mutation; **M+**, ≥1 coexisting myeloid mutation

Table 2: TKI Utilization and Discontinuation by Myeloid Mutation Status**

	M-	M+	p
Total number of TKIs used, median (IQR)	**2(1-3)**	**3(2-4)**	**<0.01**
Imatinib used, n (%)	**80 (60.2%)**	**20(83.3%)**	**0.03**
Imatinib stopped, n (%)	**65 (81.3%)**	**20 (100%)**	**0.04**
Imatinib stopped due to adverse events, n (%)	29 (44.6%)	7 (35%)	0.45
Imatinib stopped due to inadequate response or loss of response, n (%)	24 (36.9%)	10 (50%)	0.29
Ponatinib used, n (%)	**18(13.5%)**	**10(41.7)**	**<0.01**
Ponatinib stopped, n (%)	12 (66.7%)	6 (60%)	0.72
Ponatinib stopped due to adverse events, n (%)	5 (41.7%)	4(66.7%)	0.62
Ponatinib stopped due to inadequate response or loss of response, n (%)	4(33.3%)	1(16.7%)	0.62

**Second-generation TKIs and asciminib use and discontinuation did not differ between groups and are not shown

Figure 1. Mutational Landscape of Chronic Phase CML With Co-existing Mutations