Cardiac risk factors and adverse events among patients receiving first-line CLL treatment in a real-world community practice setting.

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Background: First-line (1L) ibrutinib monotherapy (IM) is commonly prescribed for CLL but is associated with cardiovascular adverse events (CVAEs) that may lead to discontinuation. Existing data are largely from clinical trials (both 1L and relapsed/refractory), and real-world evidence is limited. The aim of this study was to compare baseline cardiac risk factors and CVAEs in patients (pts) receiving 1L IM vs intensive therapy (IT; aggressive, less tolerable, majority were bendamustine plus anti-CD20 antibody) or non-intensive therapy (NIT; less aggressive, more tolerable, majority were anti-CD20 antibody alone).

Methods: We compared 3 treatment groups (IM, IT, and NIT) in terms of clinical characteristics, baseline CV risk factors, and subsequent CVAEs. Pts were selected from the Flatiron Health database based on the following criteria: aged ≥18 years, CLL/SLL diagnosis, had ≥2 clinic encounters, and initiated 1L treatment between 1/1/2016 and 12/31/2019. Baseline characteristics and subsequent CVAEs were descriptively compared between IM and IT/NIT groups; significance was assumed if $p < 0.05$.

Results: Data on 515 pts were included (IM, 191; IT, 195; NIT, 129). Age at baseline differed significantly between the IM group (mean 71.2 years) and the other 2 groups (IT, 66.2 years; NIT, 74.5 years). The proportion of del(17p) was significantly higher in the IM group vs IT/NIT groups (IM, 26.7%; IT, 3.6%; NIT, 3.1%). Significant differences between IM and IT groups were seen in baseline ECOG (ECOG 0: IM, 28.8%; IT, 43.1%), diabetes mellitus (IM, 56.0%; IT, 44.1%), and hypercholesterolemia (IM, 68.6%; IT, 58.0%). Significant differences between IM and NIT groups were seen in baseline angina/coronary revascularization (2.6% vs 8.5%), atrial fibrillation/atrial flutter (AF; 14.1% vs 26.4%), and cerebrovascular disease (8.9% vs 20.2%). The rate of any CVAE was significantly higher in IM (35.6%) vs IT and NIT groups (IT, 20.0%; NIT, 24.8%) (Table). For IM vs IT treated pts, significant differences were observed in new or worsening (N/W) AF (11.5% vs 5.1%), other arrhythmias (9.4% vs 3.1), and hypertension (HTN; 20.4% vs 8.2%).

Conclusions: This is one of the first real-world studies focused specifically on 1L CLL to describe baseline CV risk factors and compare CVAE events in CLL pts treated with IM as compared to IT or NIT. Results show higher CVAE rates of AF, other arrhythmias, and HTN for IM vs IT.

Table. CVAEs by Treatment Group

Type of CVAE	**Total (N = 515)**	**IM (n = 191)**	**IT (n = 195)**	**NIT (n = 129)**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Any cardiac toxicity	139 (27.0)	68 (35.6)	39 (20.0)*	32 (24.8)**
ACS/MI	33 (6.4)	11 (5.8)	15 (7.7)	7 (5.4)
N/W AF	39 (7.6)	22 (11.5)	10 (5.1)*	7 (5.4)
N/W other arrhythmias	30 (5.8)	18 (9.4)	6 (3.1)*	6 (4.7)
N/W heart failure	23 (4.5)	11 (5.8)	6 (3.1)	6 (4.7)
N/W HTN	71 (13.8)	39 (20.4)	16 (8.2)*	16 (12.4)

ACS/MI = acute coronary syndrome/myocardial infarction. *$p < 0.05$, IM vs IT; **$p < 0.05$, IM vs NIT.