LETTER TO THE EDITOR

CSF3R-mutated chronic neutrophilic leukemia: a two-center study of 44 consecutive patients

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Supplemental Table 1. Line of Therapy, Regimen Groups, and WBC Response in *CSF3R*-Mutated CNL Patients				
Line of Therapy	Regimen Group	Regimen (n)	N (%)	White blood cell Response* (%)
First-line (n=40)	Hydroxyurea	HU monotherapy	26 (65)	18 (78)
	HU + Ruxolitinib	HU + Ruxolitinib (1)	2 (5)	5 (62.5)
		HU + Peg-IFN + Ruxolitinib (1)		
	Ruxolitinib	Ruxolitinib alone	6 (15)	
	Others	TKI: imatinib (1) dasatinib (1)	6 (15)	NA
		IMiD (2)		
		IFN (1)		
		Azacitidine (1)		
Second-line (n=28)	Hydroxyurea alone	HU monotherapy	4 (14.3)	3 (75)
	HU + other (non-Ruxolitinib)	HU + Fedratinib	4(14.3)	
		HU + Peg-IFN		
		HU + Nilotinib		
		HU + Thalidomide		
	HU + Ruxolitinib	HU + Ruxolitinib (5)	6 (21.4)	3 (50)
		HU + Ruxo + Peg-IFN (1)		
	Ruxolitinib	Ruxo alone (4)	6 (21.4)	
		Ruxo + Busulfan (1)		
		Ruxo + Lenalidomide (1)		
	Others	Dasatinib (1)	8 (28.6)	NA
		Decitabine (3)		
		Ara-C (1) and Ara-C + 6-TG (1)		
		Azacitidine		
Third-line (n=12)	Hydroxyurea alone	HU alone (1)	3 (25)	NA
	HU + other (non-Ruxo)	HU + Decitabine (1)		
		HU + Lenalidomide (1)		
	Ruxo-based	Ruxo alone (3)	5(42)	4(100)
		Ruxo + Decitabine (1)		
		Ruxo + Peg-IFN (1)		
	Others	Daunorubicin + Cytarabine (1)	4 (33)	NA
		Decitabine alone (1)		
		Peg-IFN alone (1)		
		Cladribine (1)		

*HU – hydroxyurea; Ruxo – Ruxolitinib; Peg-IFN – pegylated interferon; TKI – tyrosine kinase inhibitor; IMiD – immunomodulatory agents; Ara-C – cytarabine; 6-TG – 6-thioguanine; NA – not available. *WBC response defined as ≥50% reduction from baseline; percentages reflect evaluable patients.*

Supplemental Table 2. Predictors of Blast Transformation and Overall Survival in *CSF3R*-Mutated CNL

	Blast transformation				**Overall Survival**			
Variable	Univariate HR (95% CI)	P value	Multivariate HR (95% CI)	P value	Univariate HR (95% CI)	P value	Multivariate HR (95% CI)	P value
Age at diagnosis > 60 years	0.67 (0.15–3.05)	0.47	–	–	5.13 (1.53–17.27)	0.008	6.30 (1.30–33.0)	0.03
Gender (M)	1.5×10^9 (NA)	0.004	3.9×10^8 (NA)	0.30	1.80 (0.76–4.26)	0.18	–	–
***CSF3R* mutations (non-T618I)**	1.22 (0.14–10.36)	0.85	–	–	0.41 (0.12–1.41)	0.16	–	–
>1 *CSF3R* mutation/variant	0.42 (0.05–3.59)	0.43	–	–	0.49 (0.17–1.44)	0.20	–	–
CSF3R variant allele frequency	0.96 (0.89–1.04)	0.28	–	–	1.00 (0.96–1.04)	0.91	–	–
Splenomegaly	2.06 (0.25–17.14)	0.50	–	–	0.91 (0.40–2.11)	0.83	–	–
Moderate/severe anemia	1.51 (0.33–6.91)	0.60	–	–	1.91 (0.88–4.12)	0.10	–	–
Platelet count <160 × 10^9/L	4.55 (0.94–22.03)	0.04	0.35 (0.05–2.10)	0.30	3.64 (1.60–8.27)	0.002	1.80 (0.70–5.10)	0.20
Leukocyte count >50 × 10^9/L	1.10 (0.20–5.80)	0.90	–	–	2.60 (1.20–5.60)	0.02	12.0 (2.60–55.0)	0.0013
Percentage Immature WBC (peripheral blood)	9.90 (1.10–93.0)	0.045	5.30 (0.53–52.8)	0.12	2.10 (0.90–4.90)	0.09	–	–
Abnormal karyotype	2.11 (0.41–10.97)	0.37	–	–	1.41 (0.52–3.85)	0.50	–	–
***ASXL1* or *SETBP1* mutation**	2.3×10^9 (NA)	0.002	2.2×10^9 (NA)	0.01	4.20 (1.20–15.0)	0.03	9.50 (1.70–58.0)	0.014
SRSF2 mutation	5.00 (0.50–48.6)	0.16	–	–	2.01 (0.71–5.70)	0.19	–	–

HR–Hazard ratio; CI – Confidence interval; NA – could not be estimated.

Supplemental Table 3. Clonal Evolution in Patients with Disease Progression/Transformation		
Events	**Number of Patients**	**Clonal Abnormalities**
CMML (Chronic Myelomonocytic Leukemia)	2	• 7p deletion (n=1) • 5q deletion and t(1;2) (n=1)
AML (Acute Myeloid Leukemia)	3	• Trisomy 21 (n=1) • Monosomy 7 (n=1) • New mutations: *NF1, PHF6, STAG2* (n=1)
CNL progression (without AML/CMML)	6	• Trisomy 21 (n=2) • Xq and 12q deletions (n=1) • del(17p), monosomy 7, *ASXL2* mutation (n=1) • Newly detected *ASXL1* mutation (n=1) • New *IDH2* mutation (n=1)