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Letter to the editor:

CONCURRENT CHRONIC MYELOID LEUKEMIA AND *CALR*-MUTATED MYELOPROLIFERATIVE NEOPLASM

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Dear Editor,

After the *JAK2* V617F mutation, insertion and/or deletion (indel) mutations of *CALR* exon 9 are the second most common driver mutations in the myeloproliferative neoplasms (MPN) of essential thrombocythemia and primary myelofibrosis and their detection is considered a major diagnostic criterion for these malignancies. It is becoming increasingly apparent that MPNs harboring *CALR* mutations (along with the mutations of *JAK2* V617F and *MPL* exon 10) may occur in patients with *BCR-ABL1*-positive chronic myeloid leukemia (CML) as evidenced by a wave of recently reported cases. The *CALR*-positive MPN and CML may appear concurrently with composite morphology or sequentially with either malignancy revealed as a consequence of specific treatment for one of the malignancies (Table 1). Review of patients shows that the presenting malignancy was unknown in one case, CML in 11/24 (46 %) and *CALR*-mutated MPN in the remaining 12/24 (50 %) cases. Evidence exists for molecular abnormalities occurring within a single clone and in distinct clonal populations.

While co-existence of CML and another MPN has clinical relevance with respect to selection and timing of tyrosine kinase inhibitor therapy, there is currently insufficient follow-up data to ascertain overall survival of such cases. There is limited value in assessing the *JAK2* V617F mutation in all newly presenting CML cases (McCarron et al., 2012): screening for the less frequent *CALR* and *MPL* mutations in all likelihood would show a similar redundancy. Given the low incidence but increasing awareness of co-existing CML and MPN, testing for the relevant rearrangement should therefore be implemented when there is clinical, hematological or morphological evidence.

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Table 1: Clinical presentation order of cases of co-existing *BCR-ABL1*-positive chronic myeloid leukemia (CML) and *CALR*-positive myeloproliferative neoplasm (MPN). ET: essential thrombocythemia; PMF: primary myelofibrosis; MF: myelofibrosis; UNK: unknown

Reference		First malignancy	Second malignancy
Pagoni et al., 2014		ET	CML
Cabagnols et al., 2015		CML	PMF
Gilles et al., 2015		CML	MPN
Bonzheim et al., 2015		ET	CML
Loghavi et al., 2015		CML	PMF
Seghatoleslami et al, 2016		CML	MPN
Diamond et al., 2016		PMF	CML
Nomani et al., 2016		PMF	CML
Dogliotti et al., 2017		CML	ET
Jeromin et al., 2017	*#1*	UNK	CML
	#2	MPN	CML
	#3	MPN	CML
Kandarpa et al., 2017	*#1*	CML	PMF
	#2	Post-ET MF	CML
Klairmont et al., 2018		MPN	CML
Lewandowski et al, 2018		CML	MPN
Blouet et al., 2018		ET	CML
De Roeck et al., 2018		Post-ET MF	CML
Boddu et al., 2018	*#1*	PMF	CML
	#2	CML	PMF
Xia et al., 2019		ET	CML
Balducci et al., 2019		CML	ET
da Costa et al., 2019		CML	MPN
Guidotti et al., 2020		CML	MPN

Conflict of interest

The author declares no conflicts of interest.

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