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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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