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Molecular screening for an underlying myeloproliferative neoplasm in patients with stroke: who and how?

TO THE EDITOR: In a recent issue of *Blood Research*, Song and colleagues highlighted the number of patients with cerebral infarctions and either erythrocytosis or thrombocytosis in whom further investigation of a myeloproliferative neoplasm (MPN) was not sought [1]. Extrapolated globally, where the lifetime risk of stroke is approximately 25%, this seemingly small number of patients with an underlying MPN would represent a considerable proportion of worldwide stroke cases in which intervention with specific MPN-directed therapies, both established and novel, would be missed [2, 3].

This important finding raises some considerations. In addition to improved communication between hematologists and neurologists, would the authors suggest implementation and justification of an MPN-associated molecular screening programme for all patients with stroke, regardless of the presence of an erythrocytosis or thrombocytosis? Furthermore, the vast majority of MPN patients presenting with stroke have molecular evidence of the *JAK2* V617F mutation, however rare cases harboring *JAK2* exon 12, *MPL* exon 10 and *CALR* exon 9 mutations have been reported [4-6]. Would the authors therefore consider incorporating these other MPN-associated driver mutations into any molecular screening programme? As MPN-directed therapy should be regarded as an integral component of secondary stroke prevention [7], identification or exclusion of this underlying malignant cause should be a priority.

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Response to the letter by Langabeer on “Retrospective screening for Philadelphia-negative myeloproliferative neoplasms in patients with cerebral infarctions as revealed using the revised 2016 World Health Organization diagnostic criteria”

TO Dr. LANGABEER: Thank you for your interests in our observations and good suggestions. Thromboembolism can precede overt presentation of a myeloproliferative neoplasm (MPN) by a few years. In this context, your suggestions on the molecular testing in stroke patients may be reasonable. Mayo Clinic has screened *JAK2V617F* in patients with 664 patients with non-splanchic thrombosis, including 136 strokes. *JAK2V617F* was found in only 6 patients, and the mutant allele burden was low in all instances (2.2–7.5%). Based on these observations, they concluded that mutation screening was not warranted as part of the hypercoagulable work-up in the absence of MPN [1]. In addition,

JAK2V617F seems to be found in normal population [2]. Furthermore, currently early detection of MPN driver gene mutations does not confer therapeutic implications in stroke patients with normal hematologic features, because available hematologic intervention such as cytoreductive therapy is indicated only in patients with overt thrombocytosis or erythrocytosis. Accordingly, we need to pay more attention to hematologic alterations at the time of diagnosis and regular follow-up of hematologic tests in patients with stroke rather than routine molecular screening, at least in daily clinical practice. For the selected cases of embolic stroke or cerebrovascular sinus thrombosis with otherwise undetermined source, molecular screening for MPN may be reasonable even in the absence of abnormal hematologic findings [3]. Collectively, molecular screening for MPN in stroke patients is still an open question, requiring prospective investigations and discussions.

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