Second primary malignancies in myeloproliferative neoplasms and the role of aspirin

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Dear Editor,

We have read the paper by Barbui et al.[1] investigating occurrence of second primary malignancies (SPM) in patients with Philadelphia chromosome negative myeloproliferative neoplasms (MPN) with great interest. Although disease- (chronic inflammation), host- (genetic background) and therapy-related factors might participate in oncogenesis of SPM in the context of MPN, pathogenesis and relevant associations for malignancies other than non-melanoma skin cancers remain poorly understood.

MPN patients are at increased risk of thrombotic incidents and are commonly given low-dose aspirin based on mostly retrospective and extrapolated data. The exception is polycythemia vera (PV) where reduced incidence of composite end point of nonfatal myocardial infarction, nonfatal stroke, pulmonary embolism, major venous thrombosis, or death from cardiovascular causes was observed with the use of aspirin in the randomized controlled trial (RCT), but without benefit regarding overall or cardiovascular mortality.[2] Aspirin is currently not considered as a drug directly affecting oncogenesis, proliferative potential, or progressive nature of MPN, which is in contrast to some other solid malignancies like colorectal cancer where it is being given miraculous preventive properties (also unsupported by robust evidence[3]). However recent ASPREE RCT[4] surprisingly reported increased cumulative incidence of cancer-related death in healthy elderly randomized to aspirin in comparison to placebo (hazard ratio 1.31; 95%CI 1.10-1.56) which was not attributable to bleeding. Results were consistent regarding different cancer types, were based on a large number of events, and supported by progressive separation of cumulative incidence curves speaking in favor of true effect rather than statistical artifact. We must therefore question ourselves whether aspirin should be taken for granted as a SPM-neutral drug in the context of MPN or it might play a similar role in SPM development.

We congratulate Barbui et al.[1] on the valuable insight into risk factors for MPN-related SPM and potential roles of different drugs. In our opinion, understanding pathogenesis of SPM would greatly benefit from considering aspirin as a potentially oncogenic or protective drug in the current and similar studies. We hope that authors can provide such aspirin-oriented analysis.

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