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Association of Platelet Thromboxane Inhibition by Low-Dose Aspirin With Platelet Count and Cytoreductive Therapy in Essential Thrombocythemia

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Abstract

Essential thrombocythemia (ET) is a myeloproliferative neoplasm characterized by enhanced platelet production and thrombotic complications. The inhibition of platelet cyclooxygenase (COX) activity by the standard once-daily aspirin is mostly incomplete due to accelerated thrombopoiesis. The phase II Aspirin Regimens in EsSential thrombocythemia (ARES) trial has recently compared the efficacy of once- vs. twice- or three-times daily low-dose aspirin in inhibiting platelet thromboxane (TX) A_2 production, as reflected by serum (s) TXB_2 measurements. The present substudy characterized the determinants of the highly variable response to the standard aspirin 100 mg once-daily regimen in fully compliant patients with ET and the effects of the experimental dosing regimens on response variability. By multivariable analysis, the platelet count (directly) and cytoreductive treatment (inversely) were significantly associated with $sTXB_2$ values in 218 patients with ET. However, the platelet count positively correlated with $sTXB_2$ in patients not being treated with cytoreductive drugs ($\rho = 0.51$, $P < 0.01$, $n = 84$), but not in patients on cytoreduction. Patients in the lowest $sTXB_2$ quartile were older, more often on cytoreductive drugs, had lower platelet count and Janus-Associated Kinase2 (JAK2)-V617F allele frequency as compared with patients in the upper $sTXB_2$ quartiles. After 2 weeks of a twice- or 3-times daily aspirin regimen, the association between the platelet count and $sTXB_2$ became similar in cytoreduced and non-cytoreduced patients. In conclusion, the platelet count appears the strongest determinant of TXA_2 inhibition by once-daily low-dose aspirin in ET, with different patterns depending of

cytoreductive treatment. More frequent aspirin dosing restores adequate platelet inhibition and reduces interindividual variability, independently of cytoreduction.

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