

Thrombosis in MPN with Thrombocytopenia Is Associated with Higher Platelet Count At the Time of the Event: Data From the Czech Registry of Patients Treated with Anagrelide,

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Abstract 3857

Background: Recent studies of prognostic parameters in Ph- myeloproliferative neoplasms with thrombocytopenia (MPN-t) indicate that WBC counts at diagnosis, rather than platelet (Plt) counts, determine the risk of thrombosis. We have studied these and other risk parameters in our patient cohort.

Patients: 843 prospectively assigned patients from the Czech segment of the International registry of patients treated with anagrelide (ANG; Thromboreductin®) were studied. The male: female ratio was 2:3, the median age was 51 (0–96) years. The majority of patients (68.1%) was pretreated by other cytoreducing drugs. According to PVSG criteria, the diagnoses were the following: essential thrombocytopenia – 569, primary myelofibrosis – 155, polycythemia vera – 92, or other – 27 patients. Data from the time of diagnosis, from the time of registry entry (at the start of ANG therapy) and from the time of the thrombotic event were evaluated. The median follow-up since registry entry was 33 (0–117) months and the follow-up comprised 2505 patient-years. All patients were treated with ANG and in 80% of follow-up reports, acetylsalicylic acid (ASA) was mentioned to be given in parallel. In 18% of entries (from registration and follow-up), administration of another cytoreducing drug (mainly hydroxyurea or interferon) in combination with ANG was noted.

Results: Of 449 thrombotic events reported, 335 occurred in history (i.e. before registry entry) and 114 during follow-up. The numbers of arterial, venous, and microcirculatory events in history were 147, 124 and 64, respectively. Of the 114 thrombotic events in 88 patients during follow-up (3.79 events/100 patient-years), 45 were classified as major. There were 61 arterial, 16 venous and 37 microcirculatory events. ANG ± ASA therapy dramatically decreased the number of venous events (7.8-fold), while arterial and microcirculatory events were reduced 2.4-fold and 1.7-fold, respectively.

At diagnosis, the strongest predictors of all thrombotic events jointly were *JAK2* V617F mutation ($P=0.001$), hereditary or acquired thrombophilia ($P<0.001$), hypertension ($P=0.006$), smoking ($P=0.02$) and diabetes mellitus ($P=0.04$). Also previous thrombosis predicted a subsequent thrombotic event ($P=0.002$). Age >65 yrs was a less powerful predictor ($P=0.08$). WBC and hematocrit levels positively correlated with the thrombotic risk ($P=0.002$ and $P=0.006$, respectively), whereas Plt counts correlated inversely with all thrombotic events ($P=0.012$) but correlated positively with microcirculatory events ($P=0.01$). Some of the factors (age, hypertension, diabetes, and smoking) powerfully predicted rather arterial events, whereas others (f.v “Leiden” mutation, protein C deficiency, elevated f.VIII levels, presence of antiphospholipid antibodies) were connected preferentially with venous events.

However, when full blood cell counts from the time of the thrombotic events were studied and compared to mean levels of all entries during follow-up, we could detect higher platelet counts at the time of the thrombotic event (454 vs 420 G/L, $P=0.007$), while we could not demonstrate any significance of the WBC counts at the time of the event. The correlation of the Plt count was marked

in all types of events and was most conspicuous in microcirculatory events. Thrombotic events during follow-up were also associated with lack of ASA therapy: only 6/16 (37.5%) patients at the time of the venous event, 35/61 (57.4%) patients at the time of the arterial event and 11/37 (29.7%) patients at the time of the microcirculatory event received ASA therapy (whereas ASA administration was reported in 80.0% of follow-up entries).

Conclusions: The current study indicates that during ANG ± ASA therapy, the incidence of thrombosis is very low in MPN-t and especially the rate of venous events is extraordinarily low. The predictors of the thrombotic events are similar as previously published by others. Above that, we have proven the usefulness of detection of the so-called thrombophilic states. However, in contrast with the prevailing current opinion, we have shown that higher platelet counts (and not WBC counts) are important at the time of thrombosis, albeit at diagnosis the Plt counts may inversely and WBC counts positively correlate with the thrombotic risk. This discrepancy may result from treatment: patients with higher Plt counts at diagnosis may receive more cytoreducing and/or antiaggregation therapy.

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