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# Euro Cancer 2018: Clonal cytogenetic abnormalities of undetermined significance - Guilin Tang - University of Texas.

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Myelodysplastic syndromes are group of hematopoietic stem cell diseases characterized by cytopenia(s), morphological dysplasia and clonal hematopoiesis. In some patients, the causes of cytopenia(s) is uncertain even after thorough clinical, laboratory evaluation. Evidence of clonal hematopoiesis has been used to support diagnosis of myelodysplastic syndrome. In patients with cytopenia(s) the presence of clonal cytogenetic abnormalities, except for +8, del (20q) –Y, can serve presumptive evidence of myelodysplastic syndrome. Recently advancements in next generation sequencing have detected myeloid neoplasm-related mutations in patients which do not meet diagnostic criteria for myelodysplastic syndrome. As various terms have been adopted that describes these cases including clonal hematopoiesis of indeterminate potential and clonal cytopenia of undetermined significance. Similarly, studies have shown that certain chromosomal abnormalities, including ones commonly detected in myelodysplastic syndrome may not be associated necessarily with an underlying myelodysplastic syndrome. These clonal cytogenetic abnormalities of undetermined significance (CCAUS) are similar to clonal hematopoiesis of indeterminate potential and clonal cytopenia of undetermined significance. Here, we review these features of CCAUS distinguishing CCAUS from clonal cytogenetic abnormalities associated with the myelodysplastic syndrome and the potential impact of CCAUS on patient management.

**Introduction:**

Polycythemia vera (PV) is a myeloproliferative neoplasm characterized by increased red blood cell production, a somatic gain-of-function mutation of JAK2, and panmyelosis in bone marrow (BM).1,2 The natural course of PV usually includes three phases: the pre-polycythemic phase, polycythemic phase (PP), and post-polycythemic myelofibrosis (post-PV MF). The disease in a small subset of patients may transform into an accelerated phase (AP), with 10–19% blasts in the peripheral blood and/or BM, or a blast phase (BP) with ≥20% blasts in peripheral blood/BM.

Patients with PV generally have relatively long survival (median, 14–19 years). Potentially fatal complications include thrombosis, progression into myelofibrosis (post-PV MF) or transformation to BP.3 The median survival for patients with post-PV MF is 5–6 years4 and patients with blastic transformation often have a dismal prognosis with a median survival of <6 months.5 The frequency of post-PV MF is 4.9–6% at 10 years and 6–14% at 15 years;3,6 and the risk of BP is 2.3–14.4% at 10 years and 5.5–18.7% at 15 years.3,7,8 Advanced age, leukocytosis, BM reticulin fibrosis, and splenomegaly have been reported to be risk factors for post-PV MF and BP;7,9–12 while leukocytosis, advanced age, and history of thrombosis have been found to be independent risk factors for overall survival (OS). Cytogenetic abnormalities can be detected in 14–20% of patients at the time of the initial diagnosis of PV,13–16 with del(20q), +8, +9 and +1q being the most commonly reported.3,17,18 The low frequency of abnormal karyotypes has made prognostication of PV patients using cytogenetic data challenging and some studies have not shown a prognostic difference between patients with a normal or abnormal karyotype.13 Recently other studies,7,14,19 including one by the International Working Group for Myeloproliferative Neoplasms Research and Treatment (IWG-MRT),7 have found that patients with an abnormal karyotype have a higher risk of disease progression and an inferior outcome. However, the prognostic impact of individual cytogenetic abnormalities was not further classified, and the three most common abnormalities, +8, +9, and del(20q) have not been shown conclusively to have prognostic value.

Here we reviewed 422 patients with PV for whom we had detailed clinicopathological and cytogenetic information. We examined the characteristics of the abnormal karyotypes during different stages of PV; the correlation of acquisition of cytogenetic abnormalities (ACA) and disease progression; and the prognostic impact of different specific cytogenetic abnormalities during different stages of PV.

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