Lack of National Consensus for the Molecular Investigation of Myeloproliferative Neoplasms

Abstract:

Sir

The discovery of the JAK2 V617F mutation ten years ago revolutionised the molecular diagnosis of the classical myeloproliferative neoplasms (MPN) of polycythaemia vera, essential thrombocythaemia and primary myelofibrosis with presence of this mutation now considered a major criteria for the diagnosis of these malignancies according to the World Health Organization classification of tumours. Despite these advances, current guidelines maintain the requirement for bone marrow aspirate and biopsy necessary for assessment of morphology and degree of fibrosis critical for therapeutic decisions. While presence or absence of this mutation is beneficial in differentiating between a reactive haematological response (causes include infection, inflammation, tissue damage, hyposplenism, haemorrhage, iron deficiency, malignancy, haemolysis and drug therapy) and a clonal MPN, testing for the JAK2 V617F mutation is becoming an advance test in the initial work up of patients for whom the aforementioned secondary causes have not been fully excluded. The year upon year increase in requests for JAK2 V617F mutation status, despite consistency in the annual number of newly diagnosed MPN patients, has been previously documented.

To assess the reasons for this increase in JAK2 V617F mutation analyses, an audit was performed on diagnostic requests from a facility for molecular testing that serves the Republic of Ireland, received between January 2006 and October 2014 inclusive. JAK2 V617F requests were analysed according to the requesting clinician/team, all of whom were from hospital Haematology departments. Requesting clinician/teams were excluded if the number of requests was less than 50 in the audit period to eliminate those with smaller practices that would not routinely request JAK2 V617F mutation analysis. A total of 8904 requests were received from 35 clinician/teams with the hit-rate calculated as the percentage of JAK2 V617F positive cases identified divided by the overall number of requests. The mutation detection methodology was unchanged throughout the audit period. The median number of requests from all clinician/teams was 193 (range 57-530) with a median "hit-rate" of 19.2%. Conspicuously, a wide range in the individual clinician/team "hit-rate" was evident, ranging from 11.2% to 41.0% (Figure 1). Of note, 4 clinician/teams (20, 23, 25 and 34) were responsible for greater than 25% of all requests, all of whom had "hit-rates" lower than the median (18.2%, 16.8%, 16.5% and 11.3% respectively).

Clearly, indications for JAK2 V617F screening vary significantly among requesting clinician/teams implying no national consensus approach to JAK2 V617F testing. Several reasons may be responsible and include non-adherence to, or unfamiliarity with, current guidelines, and ambiguity in certain clinical scenarios such as unexplained thrombosis other than splanchic vein thrombosis. Findings are to be disseminated to all clinician/teams with further audits scheduled to reassess requesting patterns. This brief but informative audit highlights the difficulties in implementing diagnostic guidelines, acknowledged to influence subsequent treatment approaches, and emphasises the need for education and adoption of consensus guidelines for the systematic investigation of a suspected MPN in the context of the discovery of new genetic markers of these diseases.

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References


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