Data-driven analysis of JAK2V617F kinetics during interferon-alpha2 treatment of patients with polycythemia vera and related neoplasms.

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Abstract

Treatment with PEGylated interferon-alpha2 (IFN) of patients with essential thrombocythemia and polycythemia vera induces major molecular remissions with a reduction in the JAK2V617F allele burden to undetectable levels in a subset of patients. A favorable response to IFN has been argued to depend upon the tumor burden, implying that institution of treatment with IFN should be as early as possible after the diagnosis. However, evidence for this statement is not available. We present a thorough analysis of unique serial JAK2V617F measurements in 66 IFN-treated patients and in 6 untreated patients. Without IFN treatment, the JAK2V617F allele burden increased exponentially with a period of doubling of 1.4 year. During monotherapy with IFN, the JAK2V617F allele burden decreased mono- or bi-exponentially for 33 responders of which 28 patients satisfied both descriptions. Bi-exponential description improved the fits in 19 cases being associated with late JAK2V617F responses. The decay of the JAK2V617F allele burden during IFN treatment was estimated to have half-lives of 1.6 year for the monoexponential response and 1.0 year in the long term for the bi-exponential response. In conclusion, through data-driven analysis of the JAK2V617F allele burden, we provide novel information regarding the JAK2V617F kinetics during IFN-treatment, arguing for early intervention.

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