The Clinical Phenotype of Myelofibrosis Encompasses a Chronic Inflammatory State that is Favorably Altered by INCB018424, a Selective Inhibitor of JAK1/2

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Abstract

Background: Myelofibrosis (MF) is characterized by elevated levels of cytokines and growth factors in patients with advanced disease. Detailed characterization of cytokine expression in MF is needed to identify potential targets for therapeutic intervention.

Methods: Plasma samples were obtained from 53 patients enrolled in the phase I/II study of INCB018424. Levels of 29 cytokines were measured in all samples using a multiplexed cytokine assay (Bio-Plex). Treatment with INCB018424 resulted in a rapid decrease of pro-inflammatory cytokines.

Results: Elevated levels of pro-inflammatory cytokines and growth factors are present in a substantial proportion of MF patients. Treatment with INCB018424 rapidly decreases pro-inflammatory cytokine levels, which is associated with improvements in constitutional symptoms and splenic volume.

Conclusions: INCB018424 is a promising therapeutic target for the treatment of MF, and its mechanism of action is consistent with the inhibition of JAK1/2. This study provides new insights into the pathophysiology of MF and suggests new therapeutic targets for this disease.