Ruxolitinib

Ruxolitinib (trade names **Jakafi** and **Jakavi**) is a drug for the treatment of intermediate or high-risk myelofibrosis, a type of myeloproliferative disorder that affects the bone marrow,[2][3] and for polycythemia vera (PCV) when there has been an inadequate response to or intolerance of hydroxyurea.[4][5]

1 Mechanism of action

Ruxolitinib is a Janus kinase inhibitor with selectivity for subtypes JAK1 and JAK2 of this enzyme.[6][7] Ruxolitinib inhibits dysregulated JAK signaling associated with myelofibrosis. JAK1 and JAK2 recruit signal transducers and activators of transcription (STATs) to cytokine receptors leading to modulation of gene expression.

2 Side effects

Side effects include thrombocytopenia (low blood platelet count), anemia (low red blood cell count) and neutropenia; risk of infection; symptom exacerbation if the medication is interrupted or discontinued; and non-melanoma skin cancer.[4][8]

Immunologic side effects have included herpes zoster (shingles) and case reports of opportunistic infections.[9] Metabolic side effects have included weight gain. Laboratory abnormalities have included alanine transaminase (ALT) abnormalities, aspartate transaminase (AST) abnormalities, and mildly elevated cholesterol levels.[4]

3 Approval

The phase III Controlled Myelofibrosis Study with Oral JAK Inhibitor-I (COMFORT-I) and COMFORT-II trials showed significant benefits by reducing spleen size and relieving debilitating symptoms.[10][11][12][13]

In November 2011, ruxolitinib was approved by the U.S. Food and Drug Administration (FDA) for the treatment of intermediate or high-risk myelofibrosis based on results of the COMFORT-I and COMFORT-II Trials.[14]

In 2014, it was approved in polycythemia vera (PCV) when there has been an inadequate response to or intolerance of hydroxyurea, based on the RESPONSE trial.[15][5]

4 Research

It is also being investigated for plaque psoriasis,[6] and for alopecia areata.[16]

In Feb 2016, a phase III trial for pancreatic cancer was terminated due to insufficient efficacy.[17]

Eight weeks-treatment with ruxolitinib blunted senescent cell-mediated inhibition of adipogenesis and increased insulin sensitivity in 22-month-old mice.[18]

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