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Syk-JAK Inhibitor PRT062070

National Cancer Institute

Source

National Cancer Institute. *Syk-JAK Inhibitor PRT062070*. NCI Thesaurus. Code C113173.

An orally bioavailable dual inhibitor of spleen tyrosine kinase (Syk) and Janus-associated kinases (JAK), with potential anti-inflammatory and antineoplastic activity. Upon oral administration, Syk-JAK inhibitor PRT062070 specifically binds to and inhibits the activity of Syk, JAK1, and JAK3 with preferential inhibition of JAK1 and JAK3-dependent cytokine-mediated signaling and functional responses. This negatively affects the downstream JAK-STAT (signal transducer and activator of transcription) pathway, and leads to both reduced inflammation in various animal models and enhanced antiproliferative activity towards non-Hodgkin's lymphoma (NHL) cell lines. Syk is a non-receptor cytoplasmic tyrosine kinase involved in signal transduction in cells of hematopoietic origin including B cells, macrophages, basophils and neutrophils. Abnormal function of Syk has been implicated in several hematopoietic malignancies including NHL and chronic lymphocytic leukemia (CLL). The JAK-STAT pathway plays a key role in the signaling of many cytokines and growth factors and is involved in cellular proliferation, growth, hematopoiesis, and the immune response; JAK kinases may be upregulated in inflammatory diseases, myeloproliferative disorders, and various malignancies.