The JAK2-targeting drug fedratinib and the BRD4 degrader dBET6 induced apoptosis and suppressed proliferation in MPN stem cells. Together, MPN stem cells display a unique phenotype, including cytokine receptors, immune checkpoint molecules, and other clinically relevant target antigens. Phenotypic characterization of neoplastic stem cells in MPN and sAML should facilitate their enrichment and the development of better, stem cell-eradicating (curative), therapies ¹⁾.

Ruxolitinib, the first JAK inhibitor approved for clinical use, improves splenomegaly and ameliorates constitutional symptoms in both myelofibrosis and polycythemia vera patients. Ruxolitinib is also useful for controlling hematocrit levels in polycythemia vera patients who were inadequately controlled by conventional therapies. Furthermore, pretransplantation use of ruxolitinib may improve the outcome of allo-hematopoietic stem cell transplantation in myelofibrosis. In contrast to these clinical merits, evidence of the disease-modifying action of ruxolitinib, i.e., reduction of malignant clones or improvement of bone marrow pathological findings, is limited, and many myelofibrosis patients discontinued ruxolitinib due to adverse events or disease progression. To overcome these limitations of ruxolitinib, several new types of JAK inhibitors have been developed. Among them, fedratinib was proven to provide clinical merits even in patients who were resistant or intolerant to ruxolitinib. Pacritinib and momelotinib have shown merits for myelofibrosis patients with thrombocytopenia or anemia, respectively. In addition to treatment for myeloproliferative neoplasms, recent studies have demonstrated that JAK inhibitors are novel and attractive therapeutic options for corticosteroid-refractory acute as well as chronic graft versus host disease ²⁾

1)

Ivanov D, Milosevic Feenstra JD, Sadovnik I, Herrmann H, Peter B, Willmann M, Greiner G, Slavnitsch K, Hadzijusufovic E, Rülicke T, Dahlhoff M, Hoermann G, Machherndl-Spandl S, Eisenwort G, Fillitz M, Sliwa T, Krauth MT, Bettelheim P, Sperr WR, Koller E, Pfeilstöcker M, Gisslinger H, Keil F, Kralovics R, Valent P. Phenotypic Characterization of Disease-Initiating Stem Cells in JAK2- or CALR-mutated Myeloproliferative Neoplasms. Am J Hematol. 2023 Feb 22. doi: 10.1002/ajh.26889. Epub ahead of print. PMID: 36814396.

Kirito K. Recent progress of JAK inhibitors for hematological disorders. Immunol Med. 2022 Oct 28:1-12. doi: 10.1080/25785826.2022.2139317. Epub ahead of print. PMID: 36305377.

From: https://neurosurgerywiki.com/wiki/ - **Neurosurgery Wiki**

Permanent link: https://neurosurgerywiki.com/wiki/doku.php?id=fedratinib



Last update: 2024/06/07 02:55