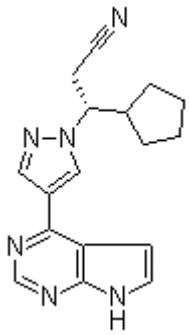
Product Introduction

Ruxolitinib (INCB018424)

INCB018424 is the first potent, selective, JAK1/2 inhibitor to enter the clinic with IC50 of 3.3 nM/2.8 nM, >130-fold selectivity for JAK1/2 versus JAK3. Phase 3.

Technical Data:

Molecular Weight (MW):	306.37
Formula:	$C_{17}H_{18}N_6$
Solubility:	DMSO ≥61mg /mL Water <1mg/mL Ethanol≥61mg/mL
Purity:	>98%
Storage:	at -20℃ 2 years
CAS No.:	941678-49-5



Biological Activity

INCB018424 potently and selectively inhibits JAK2V617F-mediated signaling and proliferation in Ba/F3 cells and HEL cells. INCB018424 markedly increases apoptosis in a dose dependent manner in Ba/F3 cells. INCB018424 (64 nM) results in a doubling of cells with depolarized mitochondria in Ba/F3 cells. INCB018424 inhibits proliferating of erythroid progenitors from normal donors and polycythemia vera patients with IC50 of 407 nM and 223 nM, respectively. INCB018424 demonstrates remarkable potency against erythroid colony formation with IC50 of 67nM. [1]

INCB018424 (180 mg/kg, orally, twice a day) results in survive rate of greater than 90% by day 22 in a JAK2V617F-driven mouse model. INCB018424 (180 mg/kg, orally, twice a day) markedly reduces splenomegaly and circulating levels of inflammatory cytokines, and preferentially eliminated neoplastic cells, resulting in significantly prolonged survival without myelosuppressive or immunosuppressive effects

in a JAK2V617F-driven mouse model. [1] The primary end point is reached in 41.9% of patients in the Ruxolitinib group as compared with 0.7% in the placebo group in the double-blind trial of myelofibrosis. Ruxolitinib results in maintaining of reduction in spleen volume and improvement of 50% or more in the total symptom score. [2] A total of 28% of the patients in the Ruxolitinib (15 mg twice daily) group has at least a 35% reduction in spleen volume at week 48 in patients with myelofibrosis, as compared with 0% in the group receiving the best available therapy. The mean palpable spleen length has decreased by 56% with Ruxolitinib but has increased by 4% with the best available therapy at week 48. Patients in the ruxolitinib group has an improvement in overall quality-of-life measures and a reduction in symptoms associated with myelofibrosis. [3]

References

http://www.cancer.gov/drugdictionary/?CdrID=593437 ;

Lawrence J Wilson. Expert Opinion on Therapeutic Patents. 2010 May;20(5):609-623.