Inhibitors, Agonists, Screening Libraries

BIOLOGICAL ACTIVITY:

Ruxolitinib (phosphate) is the first potent JAK1/2 inhibitor with IC\textsubscript{50} values of 3.3 nM/2.8 nM, more than 130-fold selectivity for JAK1/2 versus JAK3. IC\textsubscript{50} & Target: IC\textsubscript{50}: 3.3 nM (JAK1), 2.8 nM (JAK2)

In Vitro: Ruxolitinib (INCB018424) potently and selectively inhibits JAK2V617F-mediated signaling and proliferation. Ruxolitinib inhibits the growth of HEL cells with EC\textsubscript{50} of 186 nM. Ruxolitinib markedly increases apoptosis in Ba/F3-EpoR-JAK2V617F cell system, and inhibits hematopoietic progenitor cell proliferation in primary MPN patient samples\cite{1}.

In Vivo: Ruxolitinib (180 mg/kg, p.o.) reduces the tumor burden of mice inoculated with JAK2V617F-expressing cells without causing anemia or lymphopenia\cite{1}.

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: Ruxolitinib phosphate is dissolved in 0.2% DMSO\cite{1}. Cells are seeded at 2000/well of white bottom 96-well plates, treated with compounds from DMSO stocks (0.2% final DMSO concentration), and incubated for 48 hours at 37°C with 5% CO\textsubscript{2}. Viability is measured by cellular ATP determination using the Cell-Titer Glo luciferase reagent or viable cell counting. Values are transformed to percent inhibition relative to vehicle control, and IC\textsubscript{50} curves are fitted according to nonlinear regression analysis of the data using PRISM GraphPad.

Animal Administration: Ruxolitinib phosphate is dissolved in vehicle (5% dimethyl acetamide, 0.5% methocellulose).\cite{1} Mice are fed standard rodent chow and provided with water ad libitum. Ba/F3-JAK2V617F cells (10\textsuperscript{5} per mouse) are inoculated intravenously into 6- to 8-week-old female BALB/c mice. Survival is monitored daily, and moribund mice are humanely killed and considered deceased at time of death. Treatment with vehicle (5% dimethyl acetamide, 0.5% methocellulose) or Ruxolitinib (INCB018424) begins within 24 hours of cell inoculation, twice daily by oral gavage. Hematologic parameters are measured using a Bayer Advia120 analyzed, and statistical significance is determined using Dunnett testing.

References:


Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898    Fax: 609-228-5909    E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA