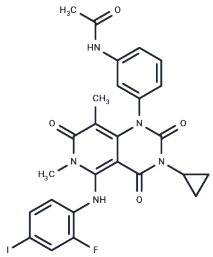
Data Sheet (Cat.No.T2125)

TargetMol

Trametinib

Chemical Properties



CAS No. : 871700-17-3

Formula: C26H23FIN5O4

Molecular Weight: 615.39

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	Trametinib (GSK1120212) is a MEK inhibitor that inhibits MEK1 and MEK2 (IC50=0.7/0.9 nM) with ATP non-competitive and oral activity. Trametinib activates autophagy and induces apoptosis.
Targets(IC50)	Apoptosis,MEK,Autophagy
In vitro	**METHODS**: Mouse intrahepatic cholangiocarcinoma cells SB1, LD-1 and human intrahepatic cholangiocarcinoma cells EGI-1 were treated with Trametinib (0-10,000 nM) for 48 h, and cell growth inhibition was detected by MTT. **RESULTS**: Trametinib dose-dependently inhibited the growth of SB1, LD-1 and EGI-1 cells with IC50 of 41.48 nM, 56.10 nM and 27.89 nM, respectively. [1] **METHODS**: Human colon cancer cells RKO were treated with Trametinib (200 nmol/L) for 30 h. The expression levels of target proteins were detected by Western Blot. **RESULTS**: Trametinib significantly reduced the levels of p-ERK and p-AKT. [2] **METHODS**: Human glioma cells U87 and U251 were incubated with Trametinib (50 nM) for 6-72 h. Apoptosis was detected by Flow Cytometry. **RESULTS**: Trametinib induced a significant increase in apoptosis in U87 and U251 cells, and Trametinib induced late apoptosis but not early apoptosis in glioma cells. [3]
In vivo	**METHODS**: To detect anti-tumor activity in vivo, Trametinib (0.3-1 mg/kg) was orally administered to BALB/c-nu/nu mice bearing human colorectal cancer tumors HT-29 and COLO205 once daily for fourteen days. **RESULTS**: Trametinib treatment significantly inhibited the growth of human colorectal cancer tumors, indicating antitumor activity in vivo. [4] **METHODS**: To assay antitumor activity in vivo, Trametinib (5 mg/kg) was injected intraperitoneally three times a week for fourteen days into NSG mice bearing human B-lymphoblastic leukemia tumors KOPN8 and COLO205. **RESULTS**: Trametinib monotherapy delayed the progression of leukemia, but was not sufficient to prevent leukemia growth. [5]
Kinase Assay	A Raf-MEK-ERK cascade kinase assay was carried out as previously described. Briefly, nonphosphorylated myelin basic protein (MBP) was coated onto an ELISA plate, and the active form of B-Raf/c-Raf was mixed with unphosphorylated MEK1/MEK2 and ERK2 in 10 μM ATP and 12.5 mM MgCl2 containing MOPS buffer in the presence of various concentrations of JTP-74057. The phosphorylation of MBP was detected by the anti-phosphoMBP antibody. Kinase inhibitory activities against a total of 99 kinases were tested by kinase profiler at 10 μM ATP [1].

Cell Research	These cells were maintained in media recommended by the providers. Exponentially growing cells were precultured in 96-well tissue culture plates for 24 h and then exposed to JTP-74057. Cell growth was determined by an in vitro toxicology assay kit, sulforhodamine B based. For combination studies, two compounds were simultaneously added to the HT-29 cells and incubated for 72 h. In the presence of various concentrations of compound A, the 50% inhibitory concentration (IC50) values of compound B were determined. Then, the fixed concentration of compound A versus the IC50 value of compound B was plotted. Conversely, the IC50 values of compound A were determined in the presence of various concentrations of compound B and plotted [1].
Animal Research	Female BALB/c-nu/nu mice were used. On day 0, HT-29 cells or COLO205 cells suspended in ice-cold HBSS (-) were inoculated subcutaneously into the right flank of the mice at 5x10^6 cells/100 µl/site or 1x10^6 cells/100 µl/site, respectively. The acetic acid-solvated form of JTP-74057 was dissolved in 10% Cremophor EL-10% PEG400 and was administered orally once daily for 14 days from the day when the mean tumor volume reached 100 mm^3. The tumor length [L (mm)] and width [W (mm)] were measured using a micro gauge twice a week after the commencement of dosing, and the tumor volume was calculated using the following formula: tumor volume (mm^3) = L x W x W/2. All procedures relating to the use of animals in this study were reviewed and approved by the Institutional Animal Care and Use Committee of Japan Tobacco [1].

Solubility Information

Solubility	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2.1 mg/mL (3.41 mM),Suspension. DMSO: 7.86 mg/mL (12.77 mM),Sonication is recommended. Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.625 mL	8.1249 mL	16.2499 mL
5 mM	0.325 mL	1.625 mL	3.250 mL
10 mM	0.1625 mL	0.8125 mL	1.625 mL
50 mM	0.0325 mL	0.1625 mL	0.325 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

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